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SPASMODIC TORTICOLLIS

II. Clinical Evaluation

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AND
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THE OCCURRENCE of involuntary motor activity of the muscles of the neck was described in 1727 by Wepfer [1] as "convulsio particularis"; but Wepfer, as well as most observers up to recent times, did not make a strict differentiation of clinical types. Classifications have been attempted, particularly by French authors, the most respected one being that of Cruchet.[2] Preconceived ideas of the etiology of "tics" and "spasm," based on definitions of Brissaud,[3] referred almost exclusively to the psychogenic nature of these conditions. As Patterson and Little [4] have stressed recently, the classification of Wilson,[5] given thirty years later, is similar to that of Cruchet; by classifying torticollis under the heading of "neuroses," Wilson showed that he still considered that psychogenic factors were the most important ones in the pathogenesis of this condition.

It was not only the lack of success of psychotherapy in the majority of cases but, rather, the universal recognition of the organic nature of the abnormal involuntary movements in nervous diseases which led to the recognition, at least in some cases, of torticollis as the symptom of an organic process of the brain, although, owing to the benign nature of the condition, only a few autopsy observations with lesions in the basal ganglia have been made in verification. Foerster,[6] in his extensive report on torticollis spasticus (1929), called attention to the fact that

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1. Wepfer, J. J.: Observationes medico-practicae, de affectibus capitis, internis et externis, Scaphusii, J. A. Ziegleri, 1727.

2. Cruchet, R: Traité des torticolis spasmodiques: Spasmes, tics, rhythmes du cou, torticolis, Paris, Masson & Cie, 1907.

3. Brissaud, E.: Leçons sur les maladies nerveuses (Salpetrière 1893-1894), Recuelliées et publiées par Henry Meigel, Paris, G. Masson, 1895.

4. Patterson, R. M., and Little, S. C.: Spasmodic Torticollis, J. Nerv. & Ment. Dis. **98**:571, 1943.

5. Wilson, S. A. K.: Neurology, edited by A. N. Bruce, Baltimore, William Wood & Company, 1940, vol. 2.

6. Foerster, O.: Torticollis Spasticus, Ztschr. f. orthop. Chir. **51**:144, 1929.

the incidence of torticollis of psychogenic origin is usually overestimated. In recent publications, since surgical treatment has brought remarkable improvement, or even symptomatic cure, in some cases, the evaluation of the importance of both psychogenic and organic factors has been attempted. The problems still to be solved were demonstrated in instructive case histories by Hyslop.[7] Differentiating in a series of cases between torticollis in the apparently psychoneurotic sphere and torticollis as part of a generalized deficiency of the nervous system, Hyslop concluded that "the causes may lie on one end of the scale purely in the psychic sphere and at the other end of the scale in a physical disease or even a developmental defect which produces structural changes in the brain."

Patterson and Little,[4] in their recent summary, correctly noted that the basic problems can be evaluated only by analysis of a large series of cases. We doubt, however, whether the statistical approach to the majority of questions involved will yield a clearcut picture in such a series of cases. In their follow-up study, these authors found that in 25 per cent of cases the condition grew worse, in 12 per cent it was unchanged, in 12 per cent it was slightly improved, in 42 per cent it was much improved and in 7 per cent it was "cured." But, without knowledge of the peculiarities of each case included in this study, one is not able to utilize this statistic in the prognosis of a given case. The same failure of statistical evaluation appears in their table of the effectiveness of the various methods of treatment. The effect of mechanical, local and physical therapy; systemic measures, and psychologic and surgical treatment can be evaluated only after consideration of the specific characteristics of each case.

SCOPE OF PRESENT INVESTIGATION

All cases with the diagnosis of spasmodic torticollis in which treatment was carried out between 1930 and 1944 at the Neurological Institute were used in this investigation. Only cases in which personal examination was possible, either at the time of the first admission to the hospital or at the occasion of the follow-up examination, were used in the final evaluation. Moving picture analyses were made in the large majority of cases, particularly before and after operation in surgically treated patients; electromyograms were taken in order to determine the participation of the various neck muscles, and psychologic tests, especially the Rorschach, were carried out, in addition to the complete neurologic examination.

7. Hyslop, G. H.: Torticollis of Central Origin, M. Clin. North America **25**:747, 1941.

In a previous communication,[8] the abnormal involuntary activity was described and an analysis of the electromyograms was given. The present paper is concerned with the clinical characteristics of the condition designated as spasmodic torticollis. In particular, the personality pattern of the patients and the extent of emotional disturbances are evaluated. In a subsequent (third) paper[9] the effect of surgical treatment in a selected group of patients will be discussed.

MATERIAL USED IN THE CLINICAL ANALYSIS

During the period from 1930 to 1944, 75 cases of a condition diagnosed as spasmodic torticollis were studied at the Neurological

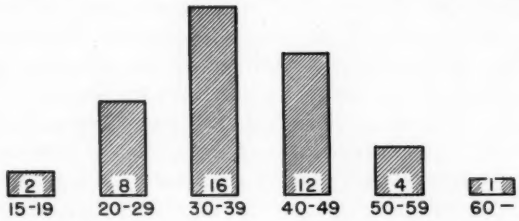

Fig. 1.—Distribution of 43 cases of torticollis on the basis of age at onset.

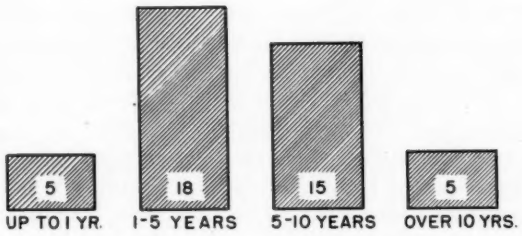

Fig. 2.—Distribution of 43 cases of torticollis on the basis of time of observation.

Institute. Forty-three patients of the original group could be examined and followed personally, and the data are therefore used for this analysis. In 25 cases treatment was medical and not surgical, and in 18 cases one or more operative procedures were performed. There were 27 male and 16 female subjects. The age at onset varied from 17 to 61 years, with the majority of patients between the ages of 30 to 50 years (fig. 1). The duration of the existence of the abnormal motor activity

8. Herz, E., and Hoefer, P. F. A.: Spasmodic Torticollis: I. Physiologic Analysis of Involuntary Motor Activity, Arch. Neurol. & Psychiat. **61**:129 (Feb.) 1949.

9. Putnam, T. J.; Herz, E., and Glaser, G. H.: Spasmodic Torticollis: III. Surgical Treatment, Arch. Neurol. & Psychiat., this issue, p. 240.

from the onset to the last observation in the group not treated surgically, and to the time of operation in the surgically treated group varied from three months to thirty-nine years (fig. 2).

CLINICAL CLASSIFICATION

Cases of "pure" torticollis are those in which abnormal involuntary motor activity of the neck muscles is the only neurologic symptom. The predominant dystonic character of this activity, as described in a previous paper,[8] induces us to use the designation "dystonic torticollis" for this condition. Occasionally, additional features were present in our series. In a few cases, although the predominant disturbance was the torticollis, there was some progression of the dystonic activity to the long muscles of the back, the muscles of the shoulder girdle and the pectoral muscles. In 2 cases (cases 26 and 31) the abnormal involuntary activity of the neck muscles was faster and more violent; it resembled choreic movements and tic twitchings, the spasms obscuring the dystonic activity. Since the neck muscles were predominantly affected, one does not seem justified in taking these cases out of the torticollis group, although the symptoms suggest a focal degenerative chorea. In another instance (case 30) definite torticollis existed; however, the late onset and the presence of parkinsonian features, especially a regular alternating tremor of the head, the somewhat masklike facies and the slowly progressing, generalized akinesia indicated the possible existence of a presenile degenerative process, such as that of idiopathic paralysis agitans. The late onset of torticollis, associated with generalized arteriosclerosis, is illustrated by another case (case 33).

Cases of torticollis with widespread dystonic involvement of other parts of the body are not included in this group. We realize that these cases might be considered instances of either late dystonia or far advanced torticollis. It was pointed out in the evaluation of a series of cases of dystonia [9a] that in cases with an onset at a later age there is a tendency to slow progression of the disease and more significant involvement of circumscribed portions of the body. The age at onset in the cases of 'true" torticollis started in the same range as that in the case of "late" dystonia; however, the peak was reached later, i.e., at the age of 30 to 40. It is noteworthy that the 2 cases (cases 29 and 32) with onset below the age of 20 were characterized by a rapid progression and relatively wide propagation of symptoms. Thus, although there is some overlapping, it is useful to distinguish between "dystonic or true torticollis" and dystonia with torticollis (the more generalized syndrome).

9b. Guillain, G., and Bize, R.: Sur un cas de sclerose en plaques avec torticolis **51**:319 (April) 1944.

Postencephalitic torticollis, and torticollis as part of the picture of multiple sclerosis (as seen in 1 case, and as described previously by Guillain and Bize [9b]) are not included in this discussion. The question of "psychogenic" or "mental" torticollis versus "true" torticollis is not raised in this classification. Later, after the case analysis, with the attempt to evaluate the importance of affective factors in dystonic torticollis, the hysterical pattern will be discussed.

The degree of torticollis, as determined by clinical evaluation in each case, was designated as mild (8 cases), medium (26 cases) or severe (9 cases). Mild torticollis was that in which there was only unilateral involvement of muscles of the neck without any notable subjective symptoms of painful tension. In cases of bilateral involvement and some subjective symptoms the torticollis was regarded as of medium degree. In severe torticollis there were bilateral involvement of the neck muscles; severe, painful tensions in the muscles, and a tendency of the hyperkinesis to spread to neighboring muscles (pectoral, long back or shoulder muscles). We realize that this classification is a rather loose one; yet its value as a clnical estimate of each case has been demonstrated.

The course of the illness was studied by evaluating the results in the nonsurgical group and those in the surgical group up to the time of operation. A static course, without improvement or with slow progression, was noted in 34 cases. The duration of the disease varied in this group, from three months to thirty-nine years, with the average duration 6.4 years. The degree of the torticollis was mild in 4, medium in 21 and severe in 9 cases. In 6 cases there was moderate improvement. The duration of illness varied from 6.5 to ten years, an average of 8.8 years, and the degree of torticollis was mild in 2 and medium in 4 cases. In 3 cases the disease was regarded as cured after a period of one and one-half, six and six and one-half years. In 2 of these cases the disease was mild, and in 1 it was of medium severity.

In 3 cases (cases 6, 9 and 34) the disease, although eventually entering a chronic, static or slightly progressive course, showed during its duration (four and one-half, eleven and thirty-one years, respectively) occasional episodes of total remission of symptoms for variable periods. The remissions seemed to be spontaneous and not readily associated with any specific circumstances. They were regarded as similar to the remissions seen occasionally in other hyperkinetic disorders, such as hepatolenticular degeneration, dystonia and myoclonus epilepsy.

9b. Guillain, G., and Bize, R.: Sur un cas de sclerose en plaques avec torticolis spasmodique, Rev. neurol. **40**:133, 1933.

The group of cases is really too small for an accurate statistical evaluation. However, certain trends can be seen. In none of the severe cases was any sign of improvement apparent. When improvement occurred (in 7 cases), the hyperkinesis was considered of medium or mild severity. Moreover, the cases in which improvement occurred had in general a longer period of observation. It should be realized that these temporal relations do not necessarily represent the natural history of the disease, since in most of the cases many forms of medical and psychiatric treatment were given. In 1 case practically complete recovery occurred without any treatment whatever.

PSYCHOGENIC FACTORS

Psychogenic factors have been regarded as important in the causation and maintenance of symptoms in spasmodic torticollis. The personality structure and the psychologic background of the patient at the onset of the disease were evaluated in our cases in an attempt to clarify the following questions:

1. Is there a predominant personality structure which predisposes to this disorder?

2. Can psychogenic factors be regarded as causative?

3. Do psychogenic factors influence the course of this illness, and by what mechanisms do they do so?

In all instances an attempt was made to distinguish between primary and secondary psychologic features; but this was often extremely difficult, as the reaction of the patient to a disorder such as this is often profound.

Personality Structure.—The personality pattern, as illustrated by the patient, and in some instances further defined by the Rorschach test, revealed abnormal trends in 27 cases. These patients were characterized as emotionally unstable, irritable, moody and sensitive, with a low affective threshold to excitement and to unpleasant or difficult situations. Maladjustments to their life situation and dissatisfaction with their accomplishments brought on difficulties in their vocation and married life. This similarity of pattern in over 50 per cent of the patients would seem to be important and worth emphasizing; yet its significance is difficult to evaluate, as will be pointed out later.

Two patients may be considered psychopathic: One (case 19) was a morphine addict, and the other (case 7) participated in doubtful business enterprises and could never make his living. Two patients (cases 7 and 13) had a low intelligence quotient. In one patient paranoid schizophrenia developed in later life, after he had been operated on for the torticollis, with some relief; another had a schizophrenic daughter.

In 14 patients no abnormal psychologic trends could be found. In 2 instances torticollis occurred twice in the same family—in a father and son, and in 2 sisters.

Evaluation of psychologic factors which might be considered of etiologic importance was rather difficult. By far the majority of patients could not elaborate any psychogenic event at the onset of the disease so remarkable that it was considered a factor responsible for the outbreak of the disorder. At least 7 patients gave a history of persistent difficulties with more or less violent psychic reactions during their entire lives. It was natural that investigation revealed a state of dissatisfaction and unbalance at the time of the onset of the disorder, although there had been many similar or equally severe reactions previously, without the development of torticollis or other symptoms of involuntary motor activity.

In 4 patients, emotional disturbances, caused by fear of losing a job, actual loss of a job, unusual mental pressure and responsibility and difficult economic problems, respectively, were rather immediate factors at the onset of the disease. But, again, these factors had been present to a variable degree before onset of the disorder, without eliciting the disorder.

The accompanying table presents the available data on the abnormal personality pattern and possible psychogenic factors at the onset of the torticollis, the severity of the disorder, the spontaneous course and the duration of the disease from the onset to the last examination or the first operation. There was no correlation at all between the degree (i.e., mild or severe) and the progression of the torticollis and the amount of psychogenic involvement. In some cases of severe, progressive disease there were few, if any, psychogenic features, while in some cases of mild form there was a strong psychogenic background. Again, there seemed to be little relation between improvement and personality pattern and the psychogenic factors at onset. The number of cases is too small to permit the evaluation of anything but general features, but of interest is the observation that in only 2 of the 7 cases in which the conditions improved was there a definite personality disturbance (cases 34 and 39) and in none of the cases was there any important psychogenic factor at the onset of the illness. In only 1 of the 3 cases of apparently spontaneous cure was an abnormal personality pattern revealed. In 2 of the latter group an occupational feature was suggested in that 1 patient was a telephone tester and another a telephone operator. However, further analysis revealed nonspecific features. In 1 case the apparent factor at onset was increasing tension and speed demanded at the job, while in the other there was a special job of watching lights and a clock which necessitated the patient's turning the head with great frequency in one direction. A physician to the New

Data on Abnormal Personality Pattern and Psychogenic Factors at Onset of Illness in 43 Cases of Torticollis

Case No.	Age at Onset, Yr.	Duration of Disorder, Yr.	Degree of Severity	Course of Illness	Abnormalities in Personality Pattern	Psychogenic Reactions at Onset	Comment
1	56	5	Medium	Static	Emotional instability	0	
2	22	5	Medium	Static	Immature; emotionally unstable	0	
3	32	3½	Mild	Static	Rorschach findings: poorly adjusted, hysterical tendencies	0	
4	36	7	Medium	Static	0	0	Two months after car accident
5	45	2½	Medium	Static	Emotionally unstable	Acute difficulties at job and in married life	Chronic dissatisfaction
6	22	31	Mild	Remittent; static	Emotionally unstable; irritable	Fear of losing job	Chronic difficulties in job and marital life
7	48	3½	Medium	Static	Psychopathic personality; emotionally unstable	Succession of unsuccessful business ventures	Intelligence quotient 85
8	31	3½	Mild	Static	Emotionally unstable and immature; duodenal ulcer	Worry about job and wife	Chronic difficulties
9	33	4½	Medium	Remittent; static	0	Change of job	Remission not associated with any particular event
10	32	10	Severe	Static; progressive (?)	0	0	
11	22	7	Medium	Static; slight improvement (?)	Immature, unstable; many phobias	Several emotional "shocks" at onset	Abnormal electroencephalogram
12	29	1	Mild	Progressive	Rorschach finding: neurotic	0	Abnormal electroencephalogram; convulsive disorder at 12; switchboard operator
13	28	½	Medium	Static	"Nervous," sensitive	0	Mentally defective, alcoholic
14	44	4	Medium	Progressive	Immature personality	Progressive tension at business	
15	43	2	Medium	Static	Emotionally unstable, maladjusted; chronic dissatisfaction	0	Chronic dissatisfaction
16	57	1	Medium	Static	Chronic anxiety	0	
17	33	3½	Severe	Static	Psychopathic personality; later schizophrenic psychosis (paranoid)	0	

No.	Yr.	Yr.	Severity	Illness			
18	43	4½	Medium	Static	Sensitive, immature	?	Unsatisfactory life
19	37	9	Medium	Static	Psychopathic personality; morphine addict	0	
20	28	1½	Medium	Static	0	0	
21	54	1½	Medium	Static, slightly progressive	0	0	
22	40	¼	Medium	Static	0	0	
23	44	4	Medium	Static	0	Loss of job	
24	47	1¼	Severe	Static	Irritable, emotionally unstable	Fatiguing work; economic problems	Daughter schizophrenic
25	49	1	Medium	Static	0	0	
26	40	5	Severe	Static	Autistic, emotionally unstable	Unusual mental pressure and responsibility	
27	31	1½	Severe	Progressive	0	0	Patient committed suicide
28	23	8½	Severe	Static	0	0	
29	17	39	Severe	Slightly progressive	"Schizoid" personality	0	
30	61	1¼	Medium	Slightly progressive	0	0	
31	47	13	Severe	Slightly progressive	Poor social adjustment; Rorschach finding: "neurotic"	0	
32	19	1½	Severe	Progressive	Emotional instability	0	
33	58	20	Medium	Static	0	0	Arteriosclerosis
34	37	11	Medium	Remittent; static	Easily excitable	First attack: "Nerves at edge"; nothing relevant to remission	
35	30	6½	Medium	Improvement	0	0	Many life difficulties
36	38	10	Medium	Improvement	?	0	Two unhappy love affairs, never married
37	38	10	Medium	Improvement	Slight emotional instability	Fall from a shelf; "head turned to the left"	
38	36	9	Mild	Improvement	0	0	
39	34	8½	Medium	Improvement	Emotional instability, psychopathic compulsive; inferiority feelings	?	Family history of psychosis, neurosis and epilepsy
40	22	9	Mild	Improvement	0	0	Sister had torticollis
41	47	1½	Mild	Cure	0	Increased tension and speed in job	Telephone tester
42	37	6	Medium	Cure	Hypochondriac, emotionally inadequate and immature	0	
43	42	6½	Mild	Cure	0	0	Telephone operator

York Telephone Company when questioned with regard to the incidence of torticollis in the employees stated that it was an extremely rare disorder.

Etiologic Significance of Psychogenic Factors.—The importance of the psychogenic factors and that of the secondary influence of these on the hyperkinesis need further elaboration. As Patterson [10] has pointed out, evaluation of the importance of psychologic factors is difficult, and the criteria of differentiation between "functional" and "organic" factors have never been well defined. One is certainly not justified, as the author stated, in regarding a torticollis as psychogenic merely because the patient presents an immature, inadequate and neurotic personality. It is interesting and important that many patients in her series, and also in ours, showed this type of personality pattern, but it must be borne in mind that such personalities are common and torticollis is uncommon, if not rare, and other causative factors must be considered. In our series the number of cases with data on psychic factors, so important that they might be considered the definitive cause of a motor psychoneurosis, is very small. Perhaps a more thorough psychiatric or psychoanalytic investigation could have elicited data of greater significance psychogenically. Yet, before further analysis of this type is undertaken, the motor manifestation of torticollis must be fully understood. It is doubtful whether the dystonic tensions of torticollis are the symbol of "turning away from life's difficulties," as has been stated frequently after the analysis of the life situation preceding the onset of the condition. Recently, Whiles [11] reported the analysis of several cases and described the factors thus: "Her symptom symbolized her previous attitude of sex, life and responsibility," or "her symptom represented her desire to turn away from people because of the repressed guilt for her father's death from heart disease," or "her symptom symbolized her attitude of turning away from her sexual role as a woman." Torticollis also has been regarded as in some way due to, or conditioned by, training movements of the head during work ("occupational" torticollis). All these conclusions are based on the assumption that the involuntary movements of the head are equivalent to the motor pattern, as in the purposive motor act of "turning away." It is true that in mild cases with contractions of one sternocleidomastoid muscle alone the resulting motion resembles a "turning or bending to one side." But the activity in most cases of torticollis, as previously described here and as illustrated by electromyograms, shows an irregular pattern, with

10. Paterson, M. T.: Spasmodic Torticollis: Result of Psychotherapy in Twenty-One Cases, Lancet **2**:556, 1945.

11. Whiles, W. H.: Treatment of Spasmodic Torticollis by Psychotherapy, Brit. M. J. **1**:969, 1940.

the participation of a variety of muscles of both sides. In addition, there is a characteristic sustained course of the single movement completely different from the movements seen in voluntary motor acts. Thus, we must conclude that the irregular sustained contractions of many different muscles of the neck in dystonic torticollis can be clearly differentiated from any pattern of purposive movements of the head.

Hysterical motor disturbances, as seen in conversion hysteria, are regarded of symbolic nature and are assumed to have a composite pattern equivalent to those observed in purposive acts. In the abnormal involuntary motor activity in organic nervous diseases, simple movements produced by the action of single muscles are the basis of the hyperkinesis. The simultaneous activity of several muscles in some instances leads to an occasional resemblance of the resulting hyperkinesis to composite purposive patterns, but one must be careful not

Fig. 3.—Patient with "hysterical" torticollis (after Redard [12]).

to draw conclusions from apparent resemblances and must attempt a careful analysis of the activity of the participating muscles.

The fact that our small series did not reveal symbolic composite motor patterns does not mean that they do not occur. For example, in an illustration from Redard [12] (fig. 3) in which a hysterical type of torticollis is pictured, the patient appears to be resting her head on the shoulder. However, in by far the majority of cases of torticollis the pattern when analyzed cannot be regarded as purposive, such as would be expected in hysterical activity or in occupational torticollis.

Influence of Emotional Factors on Involuntary Motor Activity Already Present.—This influence is undisputed. In states of excitement or "nervous tension" of any kind, the amount of involuntary

12. Redard, P.: Le torticolis et son traitement, Paris, Carré & C. Naud, 1898.

activity is increased and may spread to muscles previously not affected severely. When the apparent constitutional emotional instability in the majority of our cases is considered, it is not surprising that a time correlation between exciting circumstances and the increase of symptoms or an improvement of the torticollis after psychotherapy and after reduction of emotional strain can be routinely observed. The patient himself, of course, considers the emotional and other psychogenic factors at the onset or during the course of his condition as "the" causative factor. It seems, however, that these factors only exaggerate an organic dysfunction already present in the structure of the central nervous system. Foerster,[6] assuming with some doubt the pure psychogenic nature of torticollis in certain cases, postulated a "preexisting inferiority of the neostriatum" for these rare instances. The assumptions of Rabiner and Keschner[13] that "early functional disturbances in various segments of the body may be followed by changes in the anatomical structures," and the suggestion of Wilson, Rupp and Bartle[14] that "the emotional trauma precipitates both physiological and psychological alterations" cannot be accepted fully as yet. It would seem somewhat premature and unique to consider abnormal involuntary movements of skeletal muscles persisting over many years, as they do in torticollis, as lying in the realm of psychosomatic disorders, or to regard them as "organ neuroses," comparable to certain disorders of involuntary muscles, innervated by the vegetative nervous system. There is no indication yet that psychic factors alone can produce structural changes in the normal central nervous system. The entire subject is, however, open to further investigation.

The remarkable influence of affective and sensory stimuli on dystonic torticollis, and to some extent on all abnormal involuntary movements, is still unexplained. The amount of involuntary activity can even be diminished by sensory stimuli (counterpressure phenomenon, Wartenberg,[15] and optic or acoustic stimuli[16]). Foerster[6] offered a plausible explanation by first considering the corpus striatum as having essentially an inhibitory function. Without its restraint (i.e., as a result of pathologic lesions) the afferent stimuli constantly arriving at the

13. Rabiner, A. M., and Keschner, M.: The Role of Psychical Factors in the Production of Organic Nervous Disease, J. Neurol. & Psychiat. **10**:311, 1930.

14. Wilson, G.; Rupp, C., and Bartle, H., Jr.: Emotional Factors in Organic Disease of the Nervous System, Am. J. Psychiat. **99**:788, 1943.

15. Wartenberg, R.: Zur Klinik und Pathophysiologie der extrapyramidalen Bewegungsstörungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **83**:303, 1923.

16. Quadfasel, F.: Demonstration zur Beeinflussung des Torticollis spasticus durch sensible und sensorische Reize, Zentralbl. f. d. ges. Neurol. u. Psychiat. **62**:87, 1932. Quadfasel, F., and Krayenbuehl, H.: Ueber Haltungsstörungen und ihre Beeinflussbarkeit: Eine klinische Untersuchung bei Kranken mit Torticollis spasticus mobilis, Monatschr. f. Psychiat. **88**:39, 1934.

thalamus are conducted back into the periphery via the pallidum. Additional stimuli increase the inflow to the thalamus and, consequently, the amount of involuntary motor activity.

In studying this series of cases of torticollis, one sees therefore an entire spectrum of types of evolution: mild to severe, static, progressive, improved and remittent, and no correlation at all with the extent of psychogenic involvement. In some mild cases, there were strong emotional disturbances, whereas in other, severe and progressive, cases there was evidence of little or none. We feel that in all cases an organic disorder of the brain structure is responsible for the production of the typical involuntary movements. The clinical picture, however, may or may not be the resultant of additional conditioning by psychogenic factors, of a variable degree.

SUMMARY

Of the total number of 75 patients observed at the Neurological Institute during the period 1930 to 1944, 43 cases could be studied and followed personally.

The clinical characteristics of true "dystonic" torticollis are described. The degree of the involuntary motor activity is evaluated. The course of the disease was static in 34 cases; improvement was apparent in 6 cases; the disease was regarded as cured in 3 cases, and remissions occurred in 3 cases.

The influence of psychogenic elements as a causative factor is discussed. In over 50 per cent of the series the basic personality pattern was abnormal. A correlation between the degree and the course of torticollis and the amount of psychogenic involvement was not present. Psychologic factors did not appear of major importance at the onset of the illness.

The symbolizing explanations of torticollis on the basis of psychiatric and psychoanalytic investigations must respect the fact that the composite symbolic pattern of hysterical movements of the head is entirely different from the sustained dystonic contractions of the various muscles of the neck in torticollis.

The influence of emotional factors and sensory stimuli on the involuntary activity of the neck muscles is discussed, and a possible explanation of its genesis is offered.

It is concluded that an organic disorder of the central nervous system is responsible for the typical hyperkinesis of the neck muscles. The clinical picture may be the resultant of additional conditioning by psychogenic factors, of a variable degree.

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SPASMODIC TORTICOLLIS

III. Surgical Treatment

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A SERIES of 43 cases of spasmodic torticollis was analyzed in two previous papers [1] with respect to the physiologic mechanisms involved in the involuntary activity of the neck muscles and to the clinical characteristics. In this paper the effect of surgical treatment in 18 cases of the total series is discussed.

Many kinds of treatments have been applied in all our cases. During their long course of illness almost every patient underwent psychotherapy of various types, local physical therapy or treatment with drugs, particularly of the atropine series. It is surprising how large a percentage were in the care of chiropractors and osteopaths. Only occasional temporary improvement of the condition by one treatment or another was reported or seen during observation. In general, it may be stated that the course of the condition was not essentially altered by any kind of treatment. Our experiences are fairly similar to those of Patterson and Little.[2] Their "index of efficiency" elaborated for mechanical, local and physical therapy, for systemic measures and for psychotherapy varies to a negligible extent with each form of treatment. It is our impression that the psychologic effect of "being treated" plays an important role and that any kind of therapeutic procedure might be able to reduce the emotional lability of the patient and thus the amount of involuntary motor activity. Generally, any procedure which provides emotional relaxation will produce at least some subjective improvement, though usually only transient.

From the Department of Neurology, Columbia University, College of Physicians and Surgeons, and the Neurological Institute of New York.

1. Herz, E.; and Hoefer, P. F. A.: Torticollis: I. Physiologic and Electromyographic Analysis of Involuntary Activity, Arch. Neurol. & Psychiat. **61**:129 (Feb.) 1949. Herz, E., and Glaser, G. H.: Torticollis: II. Clinical Evaluation, ibid., this issue, p. 227.

2. Patterson, R. M., and Little, S. C.: Spasmodic Torticollis, J. Nerv. & Ment. Dis. **98**:571, 1943.

The persistent improvement in some of the nonsurgical cases could not be attributed to a particular therapeutic method; neither could the recurrence of symptoms or an apparent cure. However, one might speculate that the underlying pathologic process is not uniform. As a rule, the prognosis of the spontaneous course should respect the various possibilities: a static course; a remittent course; progression, with spread to neighboring muscles, and, in rare instances, spontaneous disappearance of the involuntary activity.

TABLE 1.—*Muscles Involved in Torticollis* *

Group 1	Muscles	Nerve Supply
Small muscles between the atlas, axis and the occiput	Rectus capitis anterior Rectus capitis lateralis Rectus capitis posterior major Rectus capitis posterior minor Obliquus capitis inferior Obliquus capitis superior	First and second cervical
	Sternocleidomastoid	Spinal accessory, second and third cervical
	Trapezius	Spinal accessory, second and third cervical
Group 2	Splenius capitis	Second and third cervical
	Splenius cervicis	Fourth to eighth cervical
Larger muscles of neck (arranged in order of importance)	Levator anguli scapulae	Third and fourth cervical
	Longissimus capitis	Second to fifth cervical
	Longissimus cervicis	Fifth to eighth cervical
	Semispinalis capitis	Second to eighth cervical
	Longus capitis	First, second and third cervical
	Scalenus anterior Scalenus medius Scalenus posterior	Second to seventh cervical
	Digastric	Fifth and seventh cranial
	Stylohyoid	Seventh cranial
Group 3	Mylohyoid	Fifth cranial
	Geniohyoid	Twelfth cranial
Muscles of deglutition, many of which play a minor role in rotation of the head and some of which are affected by section of the cervical nerves	Geniohyoglossus	Twelfth cranial
	Hyoglossus	Twelfth cranial
	Thyrohyoid	Twelfth cranial
	Sternohyoid	First, second and third cervical and twelfth cranial
	Omohyoid	First, second and third cervical and twelfth cranial
	Sternothyroid	First, second and third cervical and cranial

* After Dandy.[3]

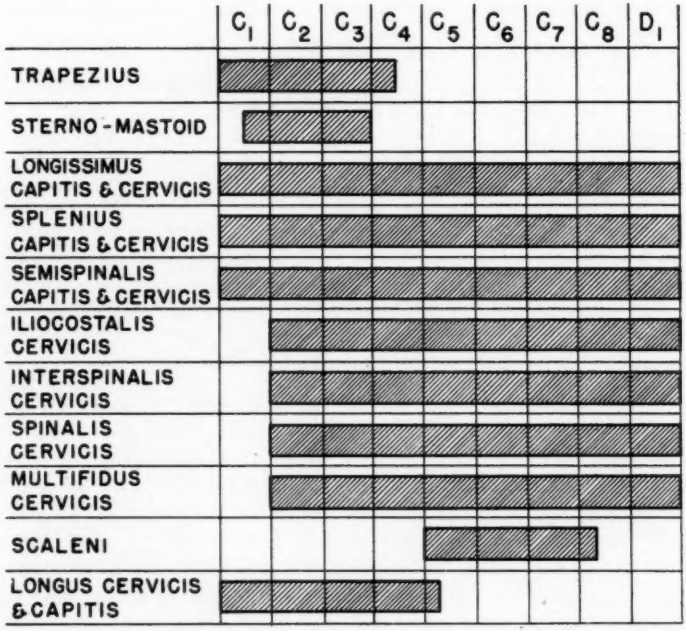
METHODS OF SURGICAL TREATMENT

The current surgical methods of treatment of spasmodic torticollis do not reduce the abnormal motor activity released by the dysfunction of the mechanisms of the brain stem. The effectiveness of the impulses is influenced only by the reduction of the strength of the participating muscles. The result of the operation primarily depends on its ability to reduce sufficiently the activity of all these muscles. For that reason, the individual variations in the involvement of the cervical muscles must be considered. In addition, individual variations in innervations of the neck muscles may influence the result of a certain surgical procedure. Table 1, showing the participation of the neck muscles in torticollis,

modified from Dandy's,[3] and the segmental spinal innervation of the most important neck muscles, reproduced from Foerster [4] (chart), are of advantage in the outline of the surgical procedure after an analysis of the distribution of the hyperkinesis in an individual case.

Three principal approaches have been applied in the surgical treatment of torticollis aimed at the elimination of the involuntary movements of the participating muscles.

1. *Myotomy.*—This method was used as early as 1641 by Isaac Minnius and was recommended by Kocher, Mikulicz and de Quervain [5]



Segmental innervation of the most important muscles of the neck (after Foerster [4]).

at the end of the last century. This method has been abandoned because denervation of the participating muscles has proved more effective and more permanent.

3. Dandy, W. E.: An Operation for the Treatment of Spasmodic Torticollis, Arch. Surg. **20**:1021 (June) 1930.

4. Foerster, O.: Spezielle Muskelphysiologie, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1937, vol. 3.

5. de Quervain, F.: Le traitement chirurgical du torticolis spasmodique d'après la méthode de Kocher, Semaine méd., **16**:405, 1896.

2. *Section of Peripheral Nerves.*—The resection of the spinal accessory nerves of the neck was first described, in 1834, by Bujalski (cited by Patterson and Little [2]). In 1891 Keen [6] divided the posterior divisions of the first three cervical nerves bilaterally. Finney and Hughson [7] used the bilateral operation of Keen together with the bilateral section of the spinal accessory nerve in the neck.

3. *Intradural Section of Cervical Roots and Spinal Accessory Fibers.*—Taylor [8] (1915) sectioned sensory roots of the first four cervical nerves. In the standard operation, as developed by Foerster [9] (1920) and Dandy [3] (1930), the anterior and posterior roots of the first three cervical nerves and the spinal accessory fibers are resected; Dandy's final recommendation was to save the sensory roots.

Dowman [10] (1931) emphasized "the necessity of varying the operative procedures to the individual case" and pointed out that "several operative procedures may have to be done before all spasmodic movements are eliminated."

PRESENT STUDY

After a careful study of the distribution of the involuntary movements in each case of the present series, three steps were contemplated:

STEP 1: The Foerster-Dandy intradural operation: bilateral section of the anterior roots of the first three cervical nerves and the spinal accessory fibers.

STEP 2: Unilateral or bilateral section of the spinal accessory nerves in the neck.

STEP 3: Keen's operation: section of the posterior divisions of the cervical nerves. As can be seen from table 1 and the chart, bilateral section of the first three anterior cervical roots and section of the spinal accessory fibers diminish the motor innervation of the trapezius and sternocleidomastoid muscles to a large extent. In mild cases, with the almost exclusive involvement of these muscles, this operation was sufficient. The amount of atrophy of these muscles varied, without apparent reason. In some instances the sternocleidomastoid and trapezius muscles of one side were much more affected and showed more complete neuromuscular degeneration than the corresponding muscles on the opposite side. It might be assumed that the intradural section of the spinal accessory fibers is not always complete and that the part the spinal accessory fibers play in the innervation of the muscles of the neck varies.

The second step, resection of the spinal accessory nerves in the neck, was first carried out on the side of the most affected muscles, and later on the contralateral

6. Keen, W. W.: New Operation for Spasmodic Wry Neck, Namely, Division or Exsection of the Nerves Supplying the Superior Rotator Muscles of the Neck, Ann. Surg. **13**:44, 1891.

7. Finney, J. M. T., and Hughson, W.: Spasmodic Torticollis, Ann. Surg. **81**:255, 1925.

8. Taylor, A. S.: Operation for Relief of Spasmodic Torticollis, in Johnson, A. B.: Operative Therapeusis, New York, D. Appleton & Company, 1915, vol. 1, p. 533.

9. Foerster, O., in discussion on Mann, L.: Torticollis Spasticus, Zentralbl. f. Chir. **47**:1106, 1920; Torticollis Spasticus, Ztschr. f. orthop. Chir. **51**:144, 1929.

10. Dowman, C. E.: Spasmodic Torticollis, Surg., Gynec. & Obst. **53**:836, 1931.

side only if necessary. Even after this resection residual spontaneous action of the neck muscles was present in some cases, probably as a result of innervation from other cervical segments or because early ramification in the course of the spinal accessory nerves makes total resection difficult.

If the long and deep cervical muscles are affected by severe tensions, section of the anterior roots of the first three cervical nerves may produce some atrophy of the upper part of these muscles, but their function seems to be maintained by additional innervation from lower segments. Particularly in the case of further progression of the disease and propagation of the dystonic disorder farther down the back, with production of a lordotic posture, is additional denervation indicated. Since the anterior divisions of the lower cervical nerves carry vital supply to the brachial plexus and diaphragm, only the posterior divisions can be resected. This was done by the method of Keen [6] and Finney and Hughson [7]; usually the posterior divisions of the fourth, fifth and sixth cervical nerves were divided. This method is less frequently used in cases of pure torticollis than in cases of dystonia with more widespread involvement of the muscles of the trunk.

RESULTS OF OPERATIVE PROCEDURES

Operation was performed in 18 cases of spasmodic torticollis. In 16 cases anterior roots of the first three cervical nerves and the spinal accessory fibers were sectioned bilaterally and in 1 case unilaterally. In 7 of these cases the additional unilateral resection, and in 2 cases the bilateral resection, of the spinal accessory nerves in the neck was carried out. In 1 case the posterior divisions of the fourth and fifth nerves were resected in addition to the intradural operation and the resection of the right spinal accessory nerve in the neck. In 1 case only the right spinal accessory nerve in the neck was resected.

Except for case 18, with a unilateral intradural operation, and case 24, with bilateral intradural operation, definite reduction of involuntary motor activity occurred. As can be seen from table 2, the degree of improvement depends on various factors, and therefore a statistical evaluation cannot be given.

First, the propagation of the dystonic movements must be taken into account. In predominantly unilateral involvement of the neck muscles, the intradural operation alone or combined with resection of the spinal accessory nerve in the neck enables the patient to hold his head straight in the majority of cases, although occasionally some tension of the affected muscles could be seen by the observer or felt by the patient. Muscles of the neck supplied by nerves other than those operated on, particularly the platysma, are naturally not influenced by these operative procedures.

Second, the course of the disease plays an important role in the operative result and its persistence. In cases 28 and 32 the involuntary activity of the neck muscles was definitely decreased by the procedures, but the dystonic tensions appeared later in the long muscles of the back and the pectoral muscles, respectively. As in case 27, the result may

TABLE 2.—*Result of Surgical Treatment in 18 Cases of Torticollis*

Case Number	Intradural Section of First Three Cervical Nerves (Anterior Roots) and Spinal Accessory Fibers	Section of Spinal Accessory Nerves	Status Before Operation	Final Result
13	+	Right +	Extreme tension, predominantly of the muscles of right side of neck	Great relaxation; only slight impairment of posture
14	+	Right +	Extreme tension, predominantly of muscles of right side of neck	Visible reduction and subjective relaxation
15	+	Right +*	Bilateral involvement of neck muscles with painful retrocollis	Much less tension but only little subjective relief admitted
16	+	—	Sustained tension of varying intensity, predominantly of muscles of right side of neck	No head movements; only slight contractions of the affected neck muscles could be seen and felt
17	+	—	Widespread bilateral activity of neck muscles, platysma and shoulder muscles	Torticollis greatly relieved; still tension of platysma
18	Left +	—	Severe tension, particularly of right sternomastoid and deep muscles of neck	Condition unchanged
19	+	—	Bilateral involvement of neck muscles with turning to left; in addition some alternating activity	Turning movements arrested; still some tention of the affected muscles
20	+	Right +	Extreme tensions, predominantly of muscles of right side of neck	Turning movements definitely reduced, but still slight involuntary activity of muscles of right side of neck
21	+	..	Tensions, particularly of muscles of right side of neck; some rhythmic activity	Great improvement, only slight instability noted
22	..	Right +	Tensions, predominantly of muscles of right side of neck	Involuntary activity appearing only with work and exercise
23	+	—	Strong tensions, predominantly of muscles of right side of neck with hypertrophy of the right sternomastoid	Head held straight; no subjective tensions felt; patient considers himself cured
24	+	—	Severe bilateral involvement, with retrocollis and alternating movements	No objective improvement
25	+	+	Bilateral involvement of neck muscles with tensions and rhythmic movements	Definite improvement but still action of deep neck muscles
26	+	—	Sustained movements in different directions; in addition, fast ticlike twitchings and rhythmic movements of neck muscles, platysma and muscles of face	Atrophy of left sternomastoid and trapezius; diminution of involuntary activity of left side more than of right side; section of right spinal accessory nerve considered
27	+	Bilateral +	Widespread disorder affecting various muscles of both sides of the neck and pectoral and shoulder muscles bilaterally	Only slight relaxation recognized; further progression; patient committed suicide
28	+	Left +	Widespread disorder affecting the neck muscles bilaterally	Relaxation of neck muscles but progression to pectoral muscles
30	+	—	Severe torsion to left; in addition, alternating tremor	After definite improvement for about 2 years, renewed appearance of severe tension with more muscles involved than before; progression of general rigidity
32	+	Bilateral +	Widespread bilateral activity of superficial and deep neck muscles with long-sustained, painful, distorted posture	Definite improvement of activity of neck muscles; head held straight; progression to long muscles of the back, resulting in intermittent lordosis

* Later the posterior divisions of the fourth and fifth cervical nerves were resected.

be completely nullified by the rapid progression of the disease, with widespread propagation of involuntary activity to the muscles of the shoulder girdle. In these cases the condition is to be considered borderline to progressive dystonia.

Third, it should be realized that in some of the cases of this series not all the steps of surgical denervation have been carried out. In some of the conditions further steps have already been suggested to the patient. Particularly, resection of the posterior divisions of the lower cervical nerves might bring additional relief in cases of the progressive type. After this series was closed, this operation was carried out in 2 additional cases, with remarkable additional relaxation.

Finally, the psychologic attitude of the patient must be taken into account even in the evaluation of the effects of operation. Case 15 is an example of the detrimental influence of a resistive attitude, produced by emotional tenseness and derangement, on the success of the operation. The patient did not recognize the definite decrease in the activity of her neck muscles and felt as much impaired as before the operation.

The indications for surgical treatment, therefore, must respect the personality pattern and the emotional situation, as well as the propagation of the involuntary activity and the course of the disease. The amount of dystonic tension that can be taken by the patient without personal impairment varies considerably. Some patients are therefore inclined to consider the surgical treatment earlier than others.

After analysis of the emotional and psychologic components, the severity and spread of the involuntary activity and the previous course of the illness, we have adopted the following attitude: In cases of a large amount of emotional involvement and only unilateral involuntary muscle activity, psychotherapeutic treatment, together with drugs of the atropine series (atropine sulfate, 1:1,000, up to 20 drops three times a day) and amphetamine sulfate (up to 10 mg. twice a day), is administered. If after a course of several months no definite improvement can be determined, the first step of the operation is suggested.

Bilateral involvement of the neck muscles with painful, severe tensions and little or no emotional background is considered a definite indication for surgical intervention.

SUMMARY

The current methods of surgical treatment of spasmodic torticollis are reviewed and their principles discussed. All procedures influence the hyperkinesis only by reducing the strength of the participating muscles.

In the present study three steps of surgical methods are contemplated: (1) the Foerster-Dandy operation; (2) unilateral or bilateral section of the accessory nerves, and (3) Keen's operation. They were carried

out (if necessary, all three; in some cases only one or two) in a series of 18 cases.

A definite reduction of involuntary activity of the neck muscles was found in 16 cases. The degree of improvement depended on various factors; these factors are discussed in detail.

The indication for surgical treatment is outlined.

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POST-TRAUMATIC VASOTHROMBOSIS

A Clinicopathologic Syndrome

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THERE are few problems in neuropathology of wider practical significance than that of the fundamental understanding of the nature and extent of cerebral lesions arising from head trauma. Both neurosurgeon and neurologist are frequently confronted with the question: What are the pathologic and physiologic changes in the brain of a patient who, after cerebral injury, complains of a great variety of neurologic or mental disturbances?

Evaluation of the degree of damage to the brain occurring in countless cases of post-traumatic invalidism is of the greatest importance, not only for the practicing physician but also for the judge and lawyer. Correct evaluation of the actual role played by trauma in such cases involves a number of questions which are not to be answered without a more profound knowledge of the widespread pathologic alterations that follow injury to the central nervous system.

In years past, a detailed study of skull fracture, meningeal hemorrhage and cerebral laceration was viewed as of paramount concern in the pathology and pathophysiology of head injuries. It is my belief, however, that any true understanding of the natural history of cerebral injuries requires consideration of the influence of the trauma on the central nervous system as a whole, in lieu of interest focused solely on local destruction confined to the surface of the brain.

Whereas the pathogenesis and pathology of the superficial tissue lacerations and hemorrhages following injury are well understood as direct sequelae of mechanical injury, little known are those diffuse tissue alterations which occur in areas remote from the direct injury. Yet there is little doubt that these diffuse cerebral changes following trauma are of the utmost practical importance.

Up to the present time, among clinicians and pathologists alike, there has prevailed the impression that alterations of the central nervous system following trauma comprise a static condition characterized by various tissue and cell reactions. The contributions of these pathologists and clinicians seem to have been restricted to establishment of a

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system of classification differentiating a few such morbid "states" as concussion, contusion and laceration. My newly proposed classification of alterations of the central nervous system following injury is based on the evolutional and dynamic principle whereby post-traumatic lesions are considered as sequential events, beginning with "functional," or reversible, changes and terminating in a series of structural pathologic syndromes.[1]

The paramount significance of diffuse vascular alterations following brain injury has been emphasized in a series of previous contributions.[2] The view has been expressed that in the early stage of injury reversible vascular changes are prevalent. One of the most frequently encountered vascular syndromes has been described under the heading of "central vasoparalysis."[3] It consists in extreme distention and engorgement of the smaller veins and capillaries associated with stasis, as evidenced by hemolysis and homogenization of red blood cells. These vascular alterations, interpreted as due to local retardation or immobilization of blood flow, are associated with an increase in permeability of the vessel wall for serous fluid and red blood cells. The perivascular spaces are maximally distended with large masses of extravasated serum and red blood cells.

It is the purpose of the present study to emphasize the significance of the vascular changes described under the heading of "vasothrombosis."[4] This report is based on a detailed study of 13 cases of cerebral injury. Three cases will be described in detail; the salient facts concerning the others will be summarized in the following section.

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1. I have described the proposed scheme of classification in detail elsewhere (Scheinker, I. M.: Neurological Pathology, Springfield, Ill., Charles C Thomas, Publisher, 1948, chap. 2).

2. Evans, J. P., and Scheinker, I. M.: Histologic Studies of the Brain Following Head Trauma: I. Posttraumatic Cerebral Swelling and Edema, J. Neurosurg. **2**:306, 1945; II. Posttraumatic Petechial and Massive Intracerebral Hemorrhage, ibid. **3**:101, 1946; III. Post-Traumatic Infarction of Cerebral Arteries with Consideration of the Associated Clinical Picture, Arch. Neurol. & Psychiat. **50**:258 (Sept.) 1943; IV. Late Changes: Atrophic Sclerosis of the White Matter, J. Neurosurg. **1**:306, 1944; V. Alterations in the Vessels of the Central Nervous System Following Trauma, A. Research Nerv. & Ment. Dis., Proc. **24**:98, 1945; VI. Post-Traumatic Central Nervous System Changes Interpreted in Terms of Circulatory Disturbances, ibid. **24**:254, 1945.

3. Scheinker, I. M.: Central Vasoparalysis: A Characteristic Vascular Syndrome and Its Significance in the Pathology of the Central Nervous System, Arch. Neurol. & Psychiat. **52**:43 (July) 1944.

4. Scheinker, I. M.: Vasothrombosis of the Central Nervous System: A Characteristic Vascular Syndrome Caused by Prolonged State of Vasoparalysis, Arch. Neurol. & Psychiat. **53**:171 (March) 1945.

REPORT OF CASES

CASE 1.—L. H. a white man aged 79, was found lying at the foot of the stairs at his home. He was brought to the hospital in an unconscious state.

Examination on his admission showed pronounced spasticity of all extremities with a bilateral Babinski sign. He was comatose and reacted only slightly to painful stimuli. The pupils were small and equal and reacted only slightly to light. His blood pressure was 150 systolic and 100 diastolic; the temperature ranged around 102 F.; the pulse rate was 100 and the respiratory rate 20 per minute (Cheyne-Stokes respiration).

On the second day of hospitalization flaccid paralysis of all extremities developed. The patient was taken to the operating room, where bitemporal, right frontal and

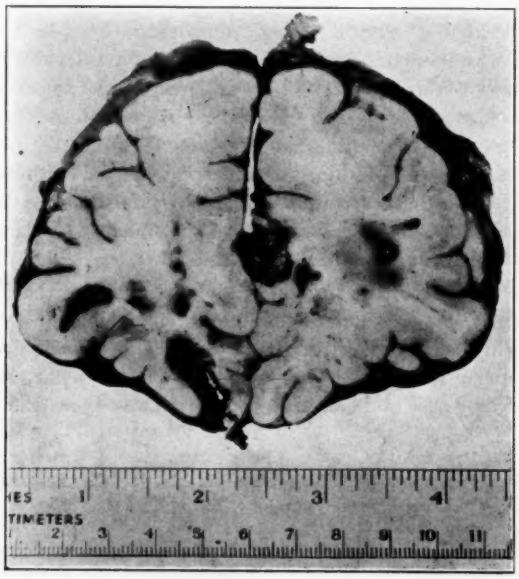

Fig. 1 (case 1).—Disseminated areas of small hemorrhages throughout the white matter of both hemispheres.

right occipital burr holes were made. A large subdural hematoma overlying the right hemisphere was encountered. Fifty cubic centimeters of clotted blood was evacuated.

The patient never regained consciousness. The postoperative course was progressively downhill and was marked by increasing respiratory distress. He died thirty hours after admission.

Autopsy, performed twelve hours after death, showed confluent lobular pneumonia, cardiac hypertrophy and dilatation and acute tracheitis.

Examination of Brain.—Gross Changes: The leptomeninges showed a diffuse hemorrhagic discoloration, most pronounced in the perisylvian regions and over the anterior tips of both frontal lobes. There were small areas of superficial contusion of the third frontal convolution on the right side and in the region of the right

olfactory bulb. There were no signs of increased intracranial pressure except for moderate fulness and slight herniation of the right uncus.

Coronal sections through both hemispheres revealed disseminated areas of petechial hemorrhages throughout both hemispheres (fig. 1). In addition there were two focal areas of hemorrhagic softening: One involved the centrum semiovale in the region of the genu of the corpus callosum: The other was located in the mesial portion of the tip of the left temporal lobe. A circumscribed area of massive hemorrhage lay in the left supracallosal gyrus. Sections through the cerebellum, brain stem and medulla revealed no abnormalities.

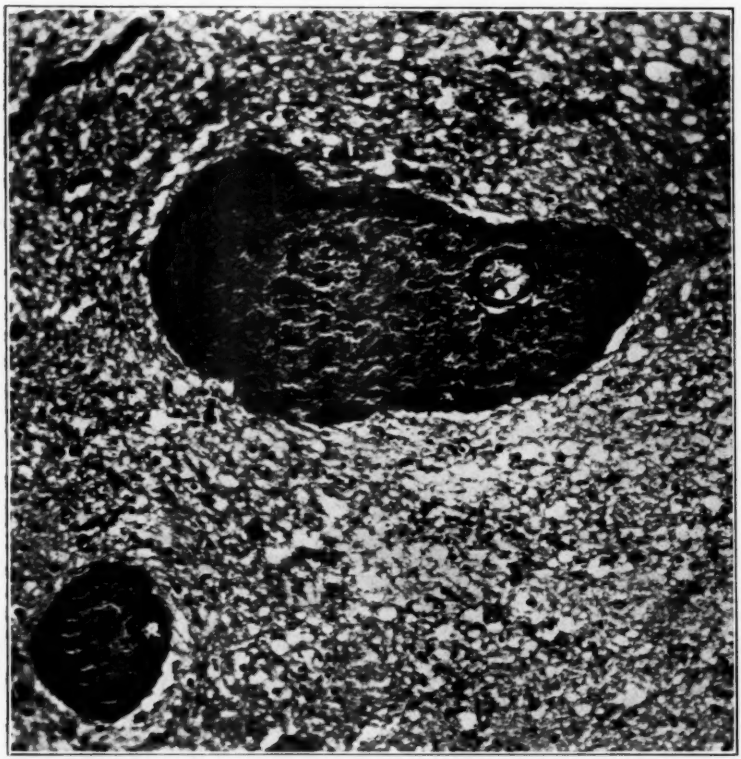

Fig. 2 (case 1).—Perivascular extravasations of blood and early stage of vasoparalysis. Hematoxylin-eosin stain; × 220.

Microscopic Changes: Histologic study of sections taken from various regions of both hemispheres disclosed two principal types of abnormality: (1) vascular alterations and (2) changes in the nervous parenchyma secondary to the circulatory disturbances.

The main histologic changes in the vascular system may be seen by reference to photomicrographs (fig. 2). What appeared to the naked eye to be petechial hemorrhages were recognized under the low power lens as perivascular extravasations of blood. The majority of the smaller veins and the capillaries were

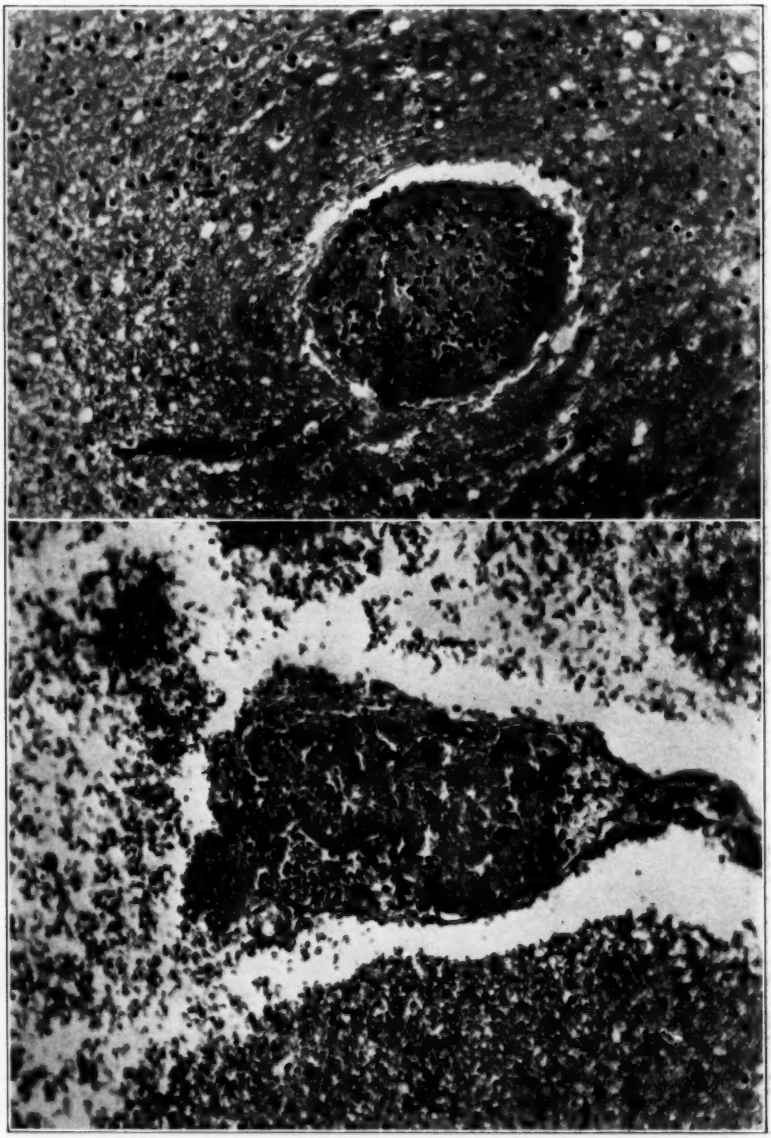

Fig. 3 (case 1).—Thrombotic occlusion of the smaller veins of the white matter. Hematoxylin-eosin stain; × 220.

tremendously distended and displayed changes characteristic of vasoparalysis. There were signs of stasis, such as homogenization of the red blood cells. These changes were frequently associated with disintegration of the vascular wall and with signs of increased permeability for serous fluid and red blood cells.

The most striking manifestation of the circulatory disturbance was the presence of various stages of venous occlusion as illustrated in figure 3. The lumens of numerous small veins and capillaries were occluded with blood clots, composed of curved strands of fibrin mixed with a large number of white and red blood cells. The clot seemed to be only slightly attached to the intima. The walls of the vessels themselves displayed various stages of degeneration and necrosis. No signs of inflammation or sclerosis could be detected.

The changes in the nerve tissue proper consisted mainly of disseminated foci of hemorrhagic softening, which were most frequently seen in those areas in which venous thrombosis occurred. The parenchyma showed signs of acute destruction of all tissue elements, without reactive glial changes. The capillaries were engorged with blood and surrounded by numerous extravasations of blood.

In addition, there were numerous small foci of anemic infarction, characterized by rarefaction of tissue and loss of stainability of the nerve parenchyma. These focal lesions were seen mostly throughout the white matter of both hemispheres.

There is little doubt that both types of focal areas of infarction (hemorrhagic and anemic) were secondary to the vascular disturbances and are to be interpreted as ischemic changes due to vascular occlusion.

Case 2.—S. J., a white man aged 29, was admitted to the hospital shortly after having been struck by an automobile and knocked unconscious.

Examination on his admission revealed deep coma and flaccid paralysis of all extremities. Both pupils were contracted and reacted to light through a small range. The left pupil was slightly larger than the right. There was no response to plantar stimulation. The blood pressure was 130 systolic and 91 diastolic; the temperature ranged around 100 F.; the pulse rate was 86 and the respiratory rate was 16 per minute.

Shortly after his admission bilateral burr holes were placed, and a small subdural hematoma (8 to 10 cc. of blood) evacuated from the left side.

After the operation there developed hyperthermia (temperature, 107 F.) and progressive irregularity of respiration. The patient died on the second day of hospitalization.

Autopsy, performed eight hours post mortem, disclosed a basal skull fracture and a small subdural hematoma on the left.

Examination of the Brain.—Gross changes: Inspection showed diffuse hemorrhagic discoloration of the leptomeninges over the right hemisphere and a small area of superficial contusion of the left temporal region. There were fulness and hemorrhagic discoloration of the uncal gyri of both temporal lobes. The cerebellum, pons and medulla were normal in appearance.

Coronal sections through both hemispheres disclosed petechial hemorrhages diffusely scattered throughout the gray and white matter of both hemispheres. Numerous foci of small hemorrhages were seen in the basal ganglia and throughout the corpus callosum. There was superficial contusion of the gray matter of the first frontal convolution of both hemispheres. Sections through the basal ganglia revealed several ball hemorrhages in the left thalamus and in the subependymal zone of both lateral ventricles.

Sections through the midbrain (fig. 4) showed numerous petechial hemorrhages confined to the tegmentum of the pons and to the periaqueductal region. In the

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region of the red nucleus and substantia nigra on each side there was evidence of swelling.

The cerebellum showed numerous petechial hemorrhages in the cortex and one well defined ball hemorrhage in the left dentate nucleus (fig. 4). In addition, there were two linear hemorrhages, each just lateral to and above the dentate nucleus.

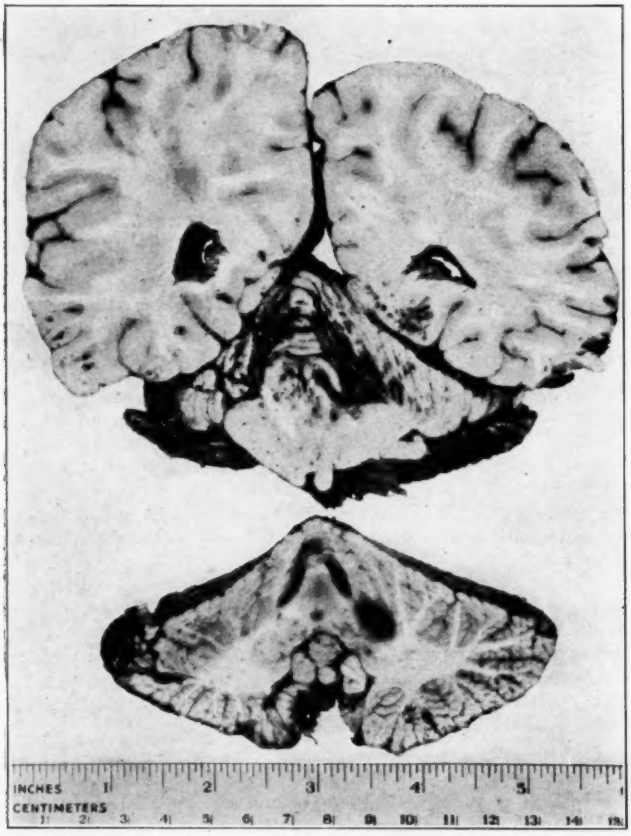

Fig. 4 (case 2).—Numerous petechial hemorrhages in the periaqueductal region and tegment of the pons. Note the cerebellar hemorrhages in the section through the dentate nuclei of the cerebellum.

Microscopic Changes: Sections taken from various regions of both hemispheres, the cerebellum and the midbrain disclosed changes similar to those described in case 1. The most striking manifestation of the circulatory disturbances was the presence of early stages of thrombosis of the smaller veins and capillaries, as illustrated in figure 5. The vascular lumens were occluded with blood clots, composed of strands of fibrin mixed with large numbers of platelets and white

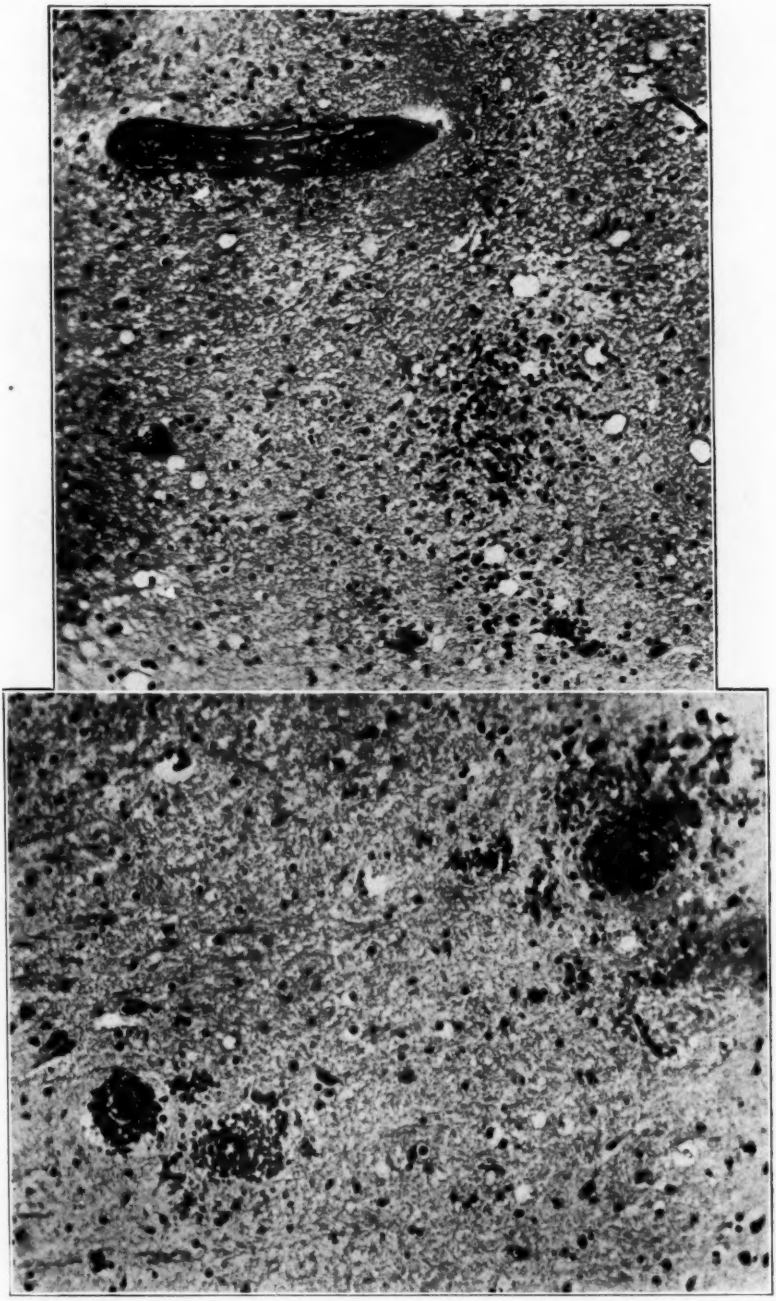

Fig. 5 (case 2).—Thrombotic occlusion of the small veins and capillaries.

blood cells. The thrombi were only slightly attached to the intima. The vascular walls showed various degrees of degeneration and necrosis. Some of the veins displayed a dense infiltration of the vascular wall with numerous white blood cells (fig. 6). These vascular changes were noted throughout scattered areas of the gray and the white matter.

In addition, numerous veins and capillaries displayed changes characteristic of various stages of vasoparalysis. They also showed signs of increased permeability of the vascular wall for serous fluid and red blood cells and were surrounded by large accumulations of extravasated red blood cells.

Fig. 6 (case 2).—Necrosis and dense infiltration with white blood cells of the wall of a small vein. Hematoxylin-eosin stain; × 180.

The nerve tissue proper displayed various stages of hemorrhagic and anemic infarction and disclosed the presence of numerous petechial and massive hemorrhages.

CASE 3.—C. J., a white man aged 60, was admitted to the hospital in a state of deep coma shortly after an automobile accident.

Examination on his admission revealed numerous prominent fractures of the lower jaw and a compound fracture of the left parietal region. Through the wound of the left parietal region brain tissue protruded. Both pupils were pinpoint in size and fixed. There was flaccid paralysis of all extremities. No reaction to plantar stimulation was obtained. The blood pressure was 130 systolic and 90 diastolic, and the pulse rate was 88 per minute. Two hours after his admission the blood

pressure dropped to 60 systolic and 0 diastolic. Administration of oxygen through the endotracheal tube and a blood transfusion raised the blood pressure to 120 systolic and 80 diastolic.

On the day of admission the patient was taken to the operating room, where the left parietal wound was debrided; fragments of bone were removed, and the dura was closed. After this procedure his temperature rose to 105 F. At 4 p. m.

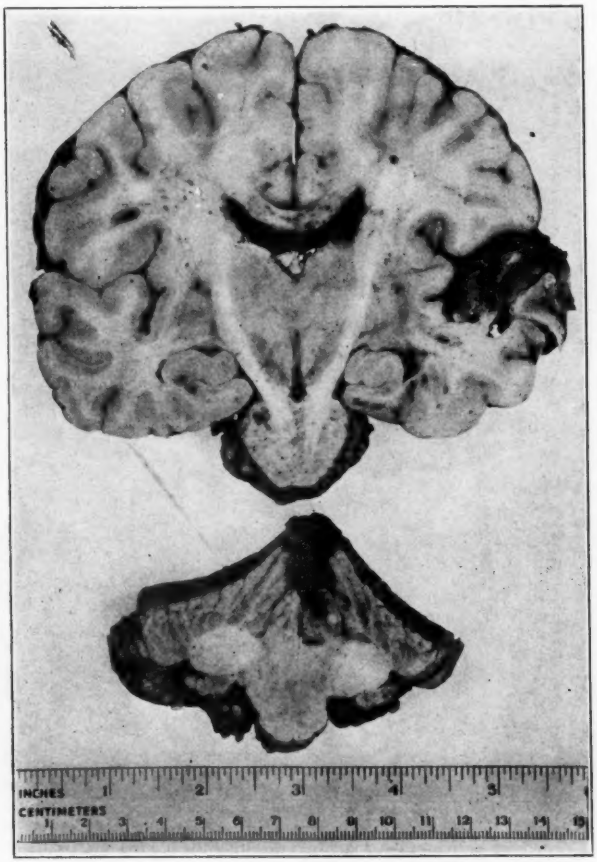

Fig. 7 (case 3).—Large number of petechial hemorrhages within the corpus callosum and the white matter of both hemispheres.

on the following day, he became cyanotic and died, approximately forty hours after admission.

Autopsy was limited to the brain.

Gross Examination.—Inspection of the brain revealed increased bulk of the right frontal region and diffuse flattening of the gyri and narrowing of the sulci of both hemispheres. The left temporal lobe appeared full and showed a superficial lacera-

tion, extending throughout the midportion of the first and second temporal convolutions. There was no true uncal herniation, although the left uncus appeared full. The cerebellum showed a well defined pressure cone, more evident on the right side than on the left. The medulla and pons were not remarkable.

Coronal sections through both hemispheres displayed a large number of petechial hemorrhages within the corpus callosum and the central white matter of both hemispheres (fig. 7). In addition, there were two extensive areas of hemorrhagic softening; one was confined to the first temporal convolution on the right, and the

Fig. 8 (case 3).—Vasoparalysis of the veins and capillaries of the white matter. Note the distended perivascular space filled with transudated serous fluid. Hematoxylin-eosin stain; × 220.

second involved the midline structures of the cerebellum. The head of the right caudate nucleus showed a well defined area of massive hemorrhage.

Sections through the brain stem displayed hemorrhagic infarction of the left brachium conjunctivum and a small number of petechial hemorrhages in the left half of the tegmentum pontis (fig. 7).

Microscopic Examination.—Sections taken from various areas of both hemispheres displayed changes almost identical with those described in cases 1 and 2. The white matter showed numerous small focal areas of hemorrhagic and anemic

infarction. These lesions varied in size and shape; many of them were small perivascular foci restricted to an area surrounding a small vein or a group of capillaries. Others were somewhat larger, involving almost an entire convolution. In almost all lesions the small blood vessels (veins and capillaries) were conspicuous because of a far advanced degree of stasis and vasoparalysis (fig. 8). The vascular walls displayed various degrees of degeneration and showed signs of increased permeability for serous fluid and red blood cells. The perivascular spaces were maximally distended and harbored large numbers of extravasated red

Fig. 9 (case 3).—Thrombotic occlusion of a vein of the central white matter. Hematoxylin-eosin stain; × 220.

blood cells. Many of the smaller veins were occluded by thrombi (fig. 8). Their walls showed signs of necrosis and were densely infiltrated with leukocytes.

COMMENT

The microscopic picture in all cases of the present series displayed circulatory disturbances of varying severity. The most pertinent changes were characterized by formation of thrombi within the tremendously distended veins and capillaries, as illustrated in figures 3, 5, and 9.

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These vascular alterations were frequently associated with vasoparalysis of the smaller blood vessels, characterized by stasis and increased permeability of the vessel walls for red blood cells and serous fluid, with resulting perivascular hemorrhages.

It seems proper to conclude that both the vasothrombosis and the vasoparalysis are varieties of the same pathophysiologic disturbance. The difference in the morphologic features can probably be best explained by the differences in severity of the circulatory changes. As has been brought out in previous papers, the state of vasoparalysis is always associated with extreme dilatation of the smaller blood vessels and with signs of stasis, characterized by hemolysis of red blood cells. Thus, the tremendous vascular distention, together with partial immobilization of the blood flow, appears to constitute the main factor contributing to the formation of vasothrombosis. Stasis and retardation of the blood flow may, in turn, lead to degenerative lesions of the endothelial lining of the veins and capillaries and thus facilitate the formation of thrombi.

In a previous paper,[4] the view was expressed that the formation of thrombi might be interpreted as a late sequela of a prolonged state of vasoparalysis, and thus may be attributed to the prolonged duration of the circulatory disturbances. The clinical data of the present study do not, however, corroborate this conclusion. As has been shown, in some cases death occurred within twenty-four to forty-eight hours after injury.

The pathophysiologic mechanism responsible for post-traumatic vasoparalysis has been discussed in detail in previous papers.[3] By way of recapitulation, their hypothetic basis may be described as follows: As the result of injury to the brain, noxious stimuli are transmitted over the neurovascular network to the smaller subdivisions of the vascular tree. These stimuli appear to cause complete relaxation or paralysis of the muscular coat of the veins and capillaries. The tremendous distention of the smaller blood vessels is associated with stasis and partial immobilization of the cerebral flow.

The slowing down of the circulation leads to the local accumulation of carbon dioxide and other metabolites. Carbon dioxide is a particularly active vasodilator. Its accumulation results in further vascular dilatation. The retarded circulation no doubt interferes with the adequate supply of oxygenated blood to the capillaries. Their walls become more permeable for serous fluid and red blood cells. The solid and fluid constituents of the blood penetrate the vessel walls. The resulting accumulation of large masses of serous fluid and red blood cells in the tremendously distended perivascular spaces serves, in turn, further to retard circulation and to contribute to the hypoxia of the nerve tissue. There seems no doubt that these physiologic

changes interfere with proper exchange of oxygen and carbon dioxide, such that the normal tissue metabolism becomes increasingly disturbed and incompatible with the maintenance of normal function.

It seems proper to conclude that the alterations of the cerebral tissue are vascular in origin and, no doubt, secondary to the circulatory disturbances. The differences in their morphologic features can probably best be explained on the basis of the type of vessel involved, whether arterial or venous. Whereas most of the petechial hemorrhages were due to increased permeability of the capillaries, the focal areas of hemorrhagic softening were caused by venous occlusion. The small focal areas of anemic infarction were probably due to an acute state of ischemia caused by immobilization of blood flow in a series of capillaries.

SUMMARY

In 13 cases of severe injury to the brain necropsy revealed circulatory disturbances characterized by thrombotic occlusion of smaller veins and capillaries, designated as vasothrombosis.

The view is expressed that the formation of thrombi is the result, in part at least, of vasoparalytic phenomena caused by transmission of force from the site of impact to the deeper structures of the brain.

It is argued, on histologic grounds, that reduction of blood flow in the occluded blood vessels and the interference with venous outflow are an adequate explanation of the pathologic alteration of the nerve parenchyma.

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ATYPICAL SYNDROMES PRODUCED BY EXTRAMEDULLARY TUMOR OF CERVICAL PORTION OF SPINAL CORD

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TUMORS of the cervical portion of the spinal cord present diagnostic difficulties which probably exceed those encountered at other levels. The close anatomic association of the cervical portion of the cord with the medulla results in the production of bizarre pictures with signs referable to both structures when the tumor lies in the upper cervical segments. Moreover, the relatively wide bony encasement of the upper cervical part of the cord permits the development of a relatively large growth without the production of a typical tumor syndrome. Finally, the location of a tumor at the proximal end of the cord, enabling it to affect all descending and ascending pathways, as well as roots mediating impulses to and from the upper limbs, permits the development of a wide variety of syndromes, which may bear close resemblances to other neurologic entities. Consequently, "classic" pictures of tumor of the cord may be found far less often than is anticipated. In view of the aforementioned difficulties, it seems worth while to present a series of cases of tumor of the cervical portion of the spinal cord in which unusual clinical pictures were displayed. They are presented in separate groups.

EXTRAMEDULLARY TUMOR OF THE CERVICAL PORTION OF THE CORD WITH NORMAL SPINAL FLUID

The diagnosis and treatment of neurologic disease were greatly facilitated by the development of more refined methods of examining the spinal fluid, both chemically and mechanically. The protein content of the cerebrospinal fluid has become recognized as one of the most sensitive indicators of neurologic disturbance and its elevation above 40 to 50 mg. per hundred cubic centimeters is a generally accepted warning to the clinician. Similarly, the discovery of the phenomenon of partial and complete subarachnoid block has provided immense aid, especially

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in the diagnosis and localization of space-taking lesions about the cord. Such determinations, followed by the subarachnoidal injection of radiopaque substances, have led to a high degree of diagnostic precision. The development of such aids, however, is not without a certain danger, for too much dependence may be placed on them and the clinician may be tempted to replace his acumen with a servile reliance on figures and formulas. Specifically, the neurologist has come to associate tumor of the spinal cord with elevation of the protein content and spinal block, especially in cases of extramedullary neoplasm. Too narrow an attitude toward this rule may encourage him to assume that a normal protein content and normal dynamics of the spinal fluid are incompatible with the presence of such tumors. In the cases to be presented, it will be seen that such an assumption is unwarranted.

CASE 1.—A student aged 20 was admitted to the private pavilion of the Mount Sinai Hospital by Dr. I. S. Wechsler in November 1945. One year before he had begun to experience dysesthesias and clumsiness in the right hand, which gradually spread upward. At the same time he was subject to attacks of sharp pains about the shoulder and neck. Subsequently, he experienced numbness of the right side of the trunk, and later of the right foot. A few months prior to his admission to the hospital he noted difficulty in walking and in the use of the right upper limb.

Examination disclosed paresis of the right upper and lower limbs, accompanied with signs of involvement of the pyramidal tract on the right side. Vibratory and position senses were impaired on that side. In the upper extremity the impairment of vibratory sense was more noteworthy on the ulnar than on the radial side. Hypesthesia and hypalgesia were noted below the fourth cervical, and to a greater degree below the third thoracic, dermatome, chiefly on the left side, the total picture suggesting a Brown-Séquard syndrome. Tenderness of the spine was noted over the third, fourth and fifth cervical vertebrae, and there was an area of hyperalgesia over the fourth cervical dermatome. Lumbar puncture revealed clear, colorless fluid, which showed no evidence of manometric block. The protein content was 12.6 mg. per hundred cubic centimeters. Roentgenographic examination of the cervical portion of the spine showed destruction of the right lamina of the fifth vertebra, with some involvement of the body. Laminectomy, performed by Dr. Ira Cohen on November 20, revealed a dumb-bell-shaped tumor arising from the anterior root of the fourth cervical nerve. The intradural portion was about the size of a small cherry; the extradural portion, which was nearly twice that size, extended through the intervertebral foramen. Pathologic examination revealed a neurofibroma. The patient was discharged practically well seven weeks later.

CASE 2.—A housewife aged 36 was admitted to the neurologic service of the Mount Sinai Hospital on Aug. 3, 1945. One year before she had begun to experience fatigue and paresthesias of the fingers of the right hand. A few months later she experienced transient weakness of the legs. By January 1945, the right arm had become numb and powerless, and paresthesias were felt on the right side of the chest, followed by weakness of the right leg. One month prior to her admission to the hospital she began to feel tingling of the left hand. She declared that she had had a cramplike pain in the back of the neck for the past four years, especially after sitting.

Examination revealed weakness in elevation of the right shoulder and some winging of the right scapula. Signs of involvement of the pyramidal tract were noted in all four limbs, especially on the right side. The sensory status was con-

fusing. Vibratory sense was absent in both lower extremities and reduced in the right upper extremity. An area of analgesia was noted from the fourth cervical to the tenth thoracic dermatome on the right side, below which there was an area of hypalgesia down to the third lumbar dermatome. Thermal sense was similarly impaired. The right pupil was smaller than the left. Inconstant nystagmoid movements were noted on lateral gaze. The spinal fluid was clear and colorless and exhibited no manometric block. The protein content was 46 mg. per hundred cubic centimeters. Iodized oil U. S. P. injected into the cisterna magna failed to descend. Roentgenograms, which on reexamination after operation showed destructive processes in the cervical vertebrae, were originally interpreted as normal. Reexamination of the sensory status ten days after her admission showed a sensory level at the second cervical dermatome. Despite the prevailing opinion that an intramedullary tumor was the most probable diagnosis, a laminectomy was performed by Dr. Ira Cohen, disclosing a large extradural tumor, which at the level of the second cervical vertabra was even extravertebral. It extended intraspinally anterior to the dura. Removal was accomplished in two stages, followed by considerable improvement. Pathologic examination revealed a neurofibroma.

In spite of the normal condition of the spinal fluid, the first case presented few diagnostic difficulties. The history of a progressive condition and the roentgenographic studies of the cervical vertebrae strongly suggested a tumor. The second case was puzzling. Not only was the roentgenographic evidence of bony destruction overlooked, but the neurologic picture was changeable and confusing. The sensory status presented the inconsistencies and variabilities more often associated with intramedullary than with extramedullary tumor. Added to these factors was that of a normal spinal fluid. The laminectomy was performed without any better indication than the chance that there might be a high cervical extramedullary tumor.

Normal spinal fluid findings in association with space-taking lesions of the cord have been described on occasion by various authors. Fleiss and Ingham [1] cited 6 cases of compression of the cord due to tumor or herniated intervertebral disk unaccompanied with manometric block of the spinal fluid. These cases included 3 of tumor at levels of from the seventh cervical to the first thoracic, the tenth thoracic and the eighth thoracic segments, respectively, and 3 of herniated disks at the fifth, fifth and fourth cervical segments. However, the protein values of the spinal fluid exceeded 100 mg. per hundred cubic centimeters in 4 of the 6 cases. In the 2 cases with both normal protein values and normal dynamic status the lesions were an extradural tumor at the tenth thoracic segment and a protruded disk at the fourth cervical segment, respectively.

In 1925 Elsberg [2] stated that 20 per cent of tumors of the spinal cord are associated with normal results in the Queckenstedt test. He revised

1. Fleiss, A. N., and Ingham, H.: Cord Compressing Lesions with Normal Queckenstedt Sign, J. A. M. A. **123**:759 (Nov. 20) 1943.

2. Elsberg, C. A.: Tumor of the Spinal Cord, New York, Paul B. Hoeber, 1925.

this estimate in 1932,[3] when, on the basis of improvement in the technic of eliciting manometric block, he asserted that of 208 cases 96 per cent showed complete or partial block. Dividing the case material according to the degree of block and the site of tumor, he provided the following tabulation[3]:

		Site of Tumor		
	All Tumors, Percentage	Extramedullary, Percentage	Intramedullary, Percentage	Extradural, Percentage
Complete block	64	71	71	51.5
Partial block	32	26.6	29	39.3
No block	4	2.4	0	9.2

Thus, he demonstrated that in his series manometric block had its highest incidence in cases of intramedullary and extramedullary tumor and the lowest in cases of extradural tumor. Conversely, patients with extradural tumor showed the highest incidence of normal dynamics of the spinal fluid.

Elsberg also declared that the spinal fluid protein measured from 150 to 450 mg. per hundred centimeters in over 80 per cent of the cases of intramedullary and extramedullary tumors, while values lying between 50 and 90 mg. per hundred cubic centimeters occurred with less than 20 per cent of these tumors. Extradural tumors, on the other hand, were oftener associated with lower protein values, between 50 and 100 mg. per hundred cubic centimeters. He stated the opinion that protein values of over 150 mg. per hundred cubic centimeters favored a diagnosis of intradural rather than of extradural tumor.

Bunts[4] found complete manometric block in 18 cases of tumor of the spinal cord, partial block in 7 cases and no block in 2 cases. In 1 of the last 2 cases the tumor was intramedullary; in the other it was both intramedullary and extramedullary. The total protein was elevated in all cases in which it was examined.

Craig and Sheldon,[5] in reviewing 68 cases of tumor of the cervical portion of the cord observed at the Mayo Clinic, found that in all but 1 instance there was evidence of either (partial or complete) manometric block or an increased total protein or of both. In only 1 case were both the dynamics of the cerebral spinal fluid and the total protein normal. They concluded that the absence of abnormality of the spinal fluid almost certainly excluded the presence of neoplasm of the cervical portion of the cord.

3. Elsberg, C. A.: The Diagnosis and Surgical Treatment of Tumor of the Spinal Cord, Cong. internat. de chir. **2**:385 (March 15-18) 1932.

4. Bunts, A. T.: Analytic Review of Thirty-Six Cases of Spinal Cord Tumors, S. Clin. North America **15**:1047 (Aug.) 1935.

5. Craig, W. M., and Sheldon, C. H.: Tumors of the Cervical Portion of the Spinal Cord, Arch. Neurol. & Psychiat. **44**:1 (July) 1940.

It is evident from the foregoing data that there is a difference of opinion concerning the spinal fluid findings in cases of tumor of the spinal cord. Although most investigators agree that some degree of block and/or some elevation of protein is the rule, the cases presented in this paper, as well as those cited by other authors, indicate important exceptions. On purely theoretic grounds it is obvious that there must be an interval in the life of such a tumor when its size or its location does not further the development of either block or protein elevation. Poppen and Hurxthal [6] came to the conclusion that the dynamic state of the cerebrospinal fluid will be normal as long as the opening around the spinal cord through which the fluid passes is as large as the bore of the lumbar puncture needle. They showed further that removal of small quantities of fluid diminishes the subarachnoid pressure sufficiently to allow the dura and arachnoid to approximate the cord, thus leading to block of the cerebrospinal fluid. They emphasized that a large tumor may exist in the absence of block.

In conclusion, despite the assertion that normal spinal fluid findings "almost certainly exclude the presence of neoplasm of the cervical cord," [5] such tumors may be found without either block or elevation of protein. From a practical point of view, this fact is of importance and should serve as a warning to the neurologic clinician not to dismiss the possibility of tumor of the cord because of normal spinal fluid findings. Whereas the presence of block and elevation of protein strongly confirm a preexisting impression of tumor of the spinal cord, their absence by no means rules it out.

EXTRAMEDULLARY NEOPLASM OF THE CERVICAL PORTION OF THE CORD WITH MINIMAL OR NO NEUROLOGIC ABNORMALITIES ON PHYSICAL EXAMINATION

The following 2 cases exhibit the difficulties in the diagnosis of tumor of the cervical portion of the cord caused by the paucity of neurologic signs.

CASE 3.—A man aged 58 began to suffer from pain on the ulnar aspect of the right elbow about four months prior to his admission to the neurologic service of the Mount Sinai Hospital, on July 31, 1945. The pain radiated down the ulnar aspect of the forearm and up to the shoulder. Mild at first, it had become severe enough later to interfere with his sleep. The patient noted some relief while sitting or standing, whereas lying down made the pain worse. It was also aggravated by coughing and sneezing. Occasionally he noted paresthesias in the painful areas. Except for some resistance to passive lateral flexion of the head to the left, the general physical and neurologic examinations showed no abnormalities. Lumbar puncture, however, revealed the presence of partial manometric block of the cerebrospinal fluid. The latter disclosed a protein content of 137 mg. per

6. Poppen, J. L., and Hurxthal, L. M.: Normal Cerebrospinal Fluid Dynamics in Spinal Cord Tumor Suspects, J. A. M. A. **103**:391 (Aug. 11) 1934.

hundred cubic centimeters. Iodized oil U. S. P. injected into the cisterna magna was partially arrested between the seventh cervical and the first thoracic vertebra. Exploration of the cervical portion of the cord by Dr. Benno Schlesinger disclosed a pear-shaped tumor lying under the arachnoid on the posterior aspect of the cord at the level of the sixth cervical vertebra. On the surface of the tumor a nerve root was spread out. After the latter was sectioned, the tumor was removed in one piece, and the patient then made a good recovery. Microscopic examination revealed the tumor to be a neurofibroma. Six months after operation the patient still noted mild pain, which, however, was far less troublesome than it had been before operation.

Several competent neurologists examined this patient and concurred in the opinion that he disclosed no neurologic abnormalities. The impression prior to the lumbar puncture was that of an unexplained mild radicular syndrome, possibly due to arthritic changes. It was only after the discovery of partial spinal fluid block and elevation of the spinal fluid protein that the diagnosis of tumor of the cervical portion of the cord was considered.

Case 4.—A man aged 63 was admitted to the neurologic service of the Mount Sinai Hospital in September 1936. For four years he had suffered from attacks of pain in the upper dorsal portion of the spine, especially when recumbent. During the nine months prior to his admission the pain had become severer and had been associated with tingling sensations down both arms. General physical examination revealed the presence of arteriosclerosis. There was no demonstrable weakness. The neurologic examination revealed a few scattered signs, which were difficult to evaluate. The deep reflexes were increased throughout. The abdominal responses were inconstant. An occasional Babinski sign was noted on the left side. A vague sensory level at the second thoracic dermatome was noted by some observers. Pressure exerted over the spines of the seventh cervical and first thoracic vertebrae produced pain. Compression of the jugular veins also produced pain, which radiated down both arms. Lumbar puncture revealed nearly complete manometric block and a protein content of 95 mg. per hundred cubic centimeters. Studies with iodized oil U. S. P. showed an arrest of the medium at the sixth cervical vertebra. A laminectomy, performed by Dr. Abraham Kaplan, disclosed a neurofibroma lying on the posterolateral aspect of the cord at that level. The tumor was attached to a sensory root. At the time of the patient's discharge from the hospital his neurologic status was normal. He remained well during a follow-up period of three years.

These 2 cases indicate that tumor formation in the cervical portion of the cord may exist despite the absence, or virtual absence, of significant neurologic signs. In both instances it was the abnormality of the spinal fluid which led to the suspicion of neoplasm. In this respect, the second group of cases stands in distinct contrast to the first. The first group exhibited striking neurologic pictures with normal spinal fluid findings, whereas the second showed little or no evidence of neurologic disorder in the presence of clearcut abnormalities of the spinal fluid.

It is common knowledge that subjective sensory disturbances may exist for a considerable length of time before any objective sensory changes are demonstrable. Elsberg [7] described a case of tumor of

7. Elsberg, C. A.: Diseases of the Spinal Cord and Its Membranes, Philadelphia, W. B. Saunders Company, 1916.

the cervical portion of the cord in which sensory disturbances were noted for the first time three days before operation. Moreover, it is evident that during the biologic history of a slow-growing mass, confined by bony walls and softer nerve tissues, the symptoms produced, the neurologic signs disclosed and the spinal fluid properties affected will generally all be functions of the size and location of the tumor. The size of the growth depends, of course, on a time factor. Consequently, at a relatively early period in the life of the growth some structures (e. g., nerve roots), may be affected, leaving others unimpaired. The location of the tumor may more readily allow it to choke off the subarachnoid space than to interfere with the functional integrity of the pyramidal tracts, and vice versa. It is reasonable to expect that in time a typical, full-blown picture of compression of the cord—symptoms, signs and changes in the spinal fluid—will develop. However, since the prognosis in such cases is immeasurably improved through early recognition, the clinician should not rely on the presence of all three elements before suspecting the presence of a tumor. The cases in group 2 illustrate with particular incisiveness the necessity for a careful evaluation of unexplained and progressive pains in the upper part of the back and the upper extremities, despite the absence of significant neurologic findings.

TUMOR OF THE CERVICAL PORTION OF THE CORD PRESENTING CLINICAL PICTURES SUGGESTIVE OF OTHER NEUROLOGIC SYNDROMES

Amyotrophic Lateral Sclerosis.—The following cases presented a clinical picture resembling that of amyotrophic lateral sclerosis.

CASE 5.—A man aged 50 was admitted to the neurologic service of the Mount Sinai Hospital in August 1937, complaining of pain in the right shoulder which had increased in severity over a period of six years. He had also noted paresthesias radiating down the right arm. Ten months prior to his admission there had developed a feeling of weakness and coldness of the right foot, which was followed by progressive weakness of both lower limbs, the right being affected more than the left. Two weeks before admission to the hospital he became unable to walk. Numbness was present in both lower extremities as high as the hips. Examination revealed tenderness over the midcervical portion of the spine and the right shoulder. The gait was paraplegic in pattern, and he required support. There was generalized wasting of the musculature, with focal atrophy of the muscles of the right lower extremity and the right deltoid area. He exhibited pronounced weakness and spasticity of the lower limbs, especially proximally. Fasciculations were noted in the muscles of the left thigh and in the right thenar eminence. There was general hyperreflexia with ankle clonus on both sides. In the upper extremities, the deep reflexes were livelier on the right side than on the left. A Babinski sign was present bilaterally. The abdominal reflexes could not be elicited. A sensory examination showed a questionable level at the sixth cervical dermatome, a finding which could not be verified by all examiners. There

was some pallhypesthesia in the lower limbs. The tongue exhibited some tremulousness, which some observers interpreted as fibrillations. On his admission, the diagnostic impression was that of vascular myelopathy or gliosis of the cervical portion of the cord associated with a syndrome resembling amyotrophic lateral sclerosis. However, lumbar puncture showed manometric block and the total protein measured 200 mg. per hundred cubic centimeters. A cisternal myelogram showed arrest of the contrast medium at the fifth cervical vertebra. A laminectomy, performed by Dr. Abraham Kaplan, disclosed a large dumbbell-shaped meningioma extending from the fifth cervical to the first thoracic vertebra and lying on the right anterolateral aspect of the cord. After removal of the tumor the patient gradually improved.

Although the history presented by this patient is not typical of amyotrophic lateral sclerosis, the neurologic picture was essentially that of the syndrome of involvement of the upper and lower motor neurons characteristic of that disease. Sensory disturbances were slight and inconspicuous, a finding which, it is to be noted, is not rare in cases of amyotrophic lateral sclerosis.

CASE 6.—A man aged 49 was admitted to the neurologic service of the Mount Sinai Hospital in August 1944, with the complaint of intermittent pain radiating to both shoulders of about one year's duration. The pain had become increasingly severe and was rendered worse on coughing and straining. During the two weeks prior to his admission rapidly progressive weakness had occurred involving both upper and lower limbs but more noticeable on the right side than on the left. Examination revealed slight tenderness over the fifth and sixth cervical spines. Tetraparesis was noted, the paralysis being more pronounced on the right side than on the left and severer distally than proximally. The interosseous muscles of both hands and the thenar and hypothenar muscles of the right hand showed atrophy. Fasciculations were noted in the hamstring muscles of the right leg. Signs of involvement of the pyramidal tract were present in all four extremities. A belt of hyperalgesia was discovered at the level of the second or third thoracic dermatome, and some examiners found a level of sensory diminution at the fourth or fifth dermatome. Vibratory sense was not present in the feet or the right leg, and it appeared to be diminished below the sixth cervical vertebra. Position sense was greatly impaired in the toes and slightly impaired in the fingers. Lumbar puncture showed complete manometric block and a protein content of 110 mg. per hundred cubic centimeters. Iodized oil U. S. P. injected into the cisterna magna was arrested at the fifth cervical vertebra. A laminectomy at this level disclosed a large herniated intervertebral disk situated between the fifth and the sixth vertebra on the right side. Operation was followed by gradual improvement in both motor and sensory functions.

While the presence of root pain and a questionable sensory level suggested the diagnosis of an extramedullary tumor, the outstanding neurologic signs pointed to an upper and lower motor neuron lesion characteristic of the syndrome of amyotrophic lateral sclerosis. The changes in the spinal fluid, however, strengthened the impression of tumor.

Cases of syndromes resembling amyotrophic lateral sclerosis caused by compressing lesions of the cervical portion of the spinal cord have

occasionally been reported. Garcin and associates,[8] in 1933, described the case of a man aged 48 who at the onset of his illness presented an almost classic picture of amyotrophic lateral sclerosis, followed later by the development of a sensory level at the second thoracic dermatome. Exploration revealed a tumor of the cervical portion of the cord after the removal of which the patient made a complete recovery. More recently, de Lehoczky and Piri[9] described a tumor of the cervical portion of the cord associated with a syndrome resembling amyotrophic lateral sclerosis in a youth aged 16 who presented no significant sensory disturbances and no abnormality of either the dynamic status or the protein content of the spinal fluid. The correct diagnosis was made through the discovery of an enlarged intervertebral foramen in a roentgenogram of the neck and the presence of a palpable tumor in the supraclavicular fossa.

The mechanism whereby a tumor of the cervical portion of the cord is capable of producing a syndrome resembling amyotrophic lateral sclerosis is a matter of speculation. It is of interest to note that in virtually all cases reported in the literature the tumor was located on the anterior or anterolateral aspect of the cord. In the cases presented in this paper the localization was similar.

In a recent paper, Kahn,[10] presenting 2 cases of herniated cervical disk producing the clinical picture of so-called lateral sclerosis, discussed the selective involvement of the pyramidal tracts by anteriorly placed tumors. Citing the work of Gasser and Erlanger, who found that compression of a peripheral nerve affected the fibers in the order of their size, Kahn suggested that a similar mechanism is at work in compression of the cord, with the result that the thinner spinothalamic fibers are less susceptible to ischemia than the coarser fibers of the pyramidal tracts and the posterior columns. If pressure were transmitted equally in all directions, the latter two pathways would, on this basis, be affected earlier by a compressing lesion than the spinothalamic tracts. However, as Kahn pointed out, anteriorly placed tumors do not exert pressure equally in all directions, since the dentate ligament tends to anchor the anterolateral aspect of the cord. Consequently, a tumor situated on the anterior or the anterolateral aspect of the cord tends to affect the fibers of the pyramidal tract before those of the spinothalamic pathways because of the larger size

8. Garcin, R.; Petit-Dutaillis, D.; Bértrand-Fontaine, and LaPlane, J.: Tumeur de la moelle cervicalle evoluant sous les traits d'une sclérose latérale amyotrophique, Rev. neurol. **1**:391 (March) 1933.

9. de Lehoczky, T., and Piri, L.: Syndrome of Amyotrophic Lateral Sclerosis Caused by Cervical Hour-Glass Tumor, Confinia neurol. **6**:71, 1944.

10. Kahn, E. A.: The Role of the Dentate Ligaments in Spinal Cord Compression and the Syndrome of Lateral Sclerosis, J. Neurosurg. **4**:191 (May) 1947.

of the former, and before the fibers of the posterior columns because of the greater mechanical stress to which the pyramidal tracts are subjected. That the pyramidal pathways are notoriously susceptible to a variety of agents is attested to by the ease with which the Babinski sign may be induced. At the same time, it is not altogether clear why the anterior horn cells should be affected bilaterally by such tumors, particularly in cases in which the tumor appears to be remote from the affected myotomes.

Cases such as those reported in this paper, as well as cases cited from the literature, serve as a reminder that the mere presence of a syndrome resembling amyotrophic lateral sclerosis does not necessarily imply the presence of primary amyotrophic lateral sclerosis. Wechsler's [11] division of the disease into "syndromes of varying etiology" finds ample justification in the material presented here and emphasizes the necessity of one's thinking in terms of various diagnostic possibilities before condemning the patient to the hopeless prognosis of true amyotrophic lateral sclerosis.

Posterolateral Sclerosis.—The clinical picture in the following case resembles that of posterolateral sclerosis.

CASE 7.—A woman aged 49 was admitted to the neurologic service of the Mount Sinai Hospital on Sept. 6, 1946, with a history of nervousness and fatigability of six years' duration and of paresthesias and numbness of the right hand beginning eighteen months prior to admission. Within the year before entering the hospital she had noted similar sensations in the left hand and in both feet. An unsteady gait, clumsiness in performing skilled movements and urinary frequency with occasional incontinence had been present for about six months. Kyphoscoliosis had been present for many years. Examination revealed a broad-based, ataxic gait. Movements in the finger to nose and heel to knee tests were performed unsteadily. There was weakness of both upper extremities; the deep reflexes were hyperactive, and the Hoffmann and Babinski signs were elicited bilaterally. The abdominal cutaneous reflexes were not elicited. A slight hypalgesia was noted over the radial border of the right hand and forearm. Superficial sensation was otherwise intact. Vibratory sensation was diminished in both upper limbs, especially on the right side, and was absent in both lower limbs and trunk as high as the thoracic region. Position sense was moderately impaired in the toes and conspicuously so in the fingers. Dysgraphesthesia and astereognosis were present in the right hand. Examination of the blood disclosed moderate secondary anemia, without evidence of pernicious anemia. Free hydrochloric acid was present in the gastric juice after the administration of histamine. Lumbar puncture revealed the presence of complete manometric block and a protein content of 87 mg. per hundred cubic centimeters. A roentgenogram of the cervical portion of the spine showed an enlargement of the intervertebral foramen between the sixth and the seventh vertebra on the right side, associated with erosion of the posterolateral aspect of the vertebral bodies. A laminectomy was performed by Dr. Ira Cohen, and a large dumbbell-shaped tumor (neurofibroma) which appeared to originate in

11. Wechsler, I. S.: Textbook of Clinical Neurology, ed. 5, Philadelphia, W. B. Saunders Company, 1943, p. 126.

the right sixth anterior root was removed. After this procedure the patient exhibited gradual improvement in both motor and sensory functions.

The initial impression created by this clinical picture was that of intramedullary disease of the cord presenting the syndrome of posterolateral sclerosis. Both hematologic studies and gastric analysis precluded the diagnosis of pernicious anemia. The spinal puncture pointed strongly to the possibility of tumor, an impression which was confirmed by the roentgenographic findings.

Friedman,[12] in 1939, published a review of the subject of tumors of the cervical portion of the cord presenting the picture of combined system disease, in which he described 3 cases of his own, as well as 7 previously reported by himself, Néri,[13] Roussy and Levy[14] and Schick. While in 2 of the 3 cases described by Néri the tumor was ventrally placed, in the majority of the cases, including our own, the tumor was on the posterior aspect of the cord. Friedman suggested that the signs of involvement of the posterior column exhibited by posteriorly placed tumors were due to direct pressure, while those associated with anteriorly situated growths were caused by contrecoup pressure. He was inclined to explain the severer involvement of the posterior columns as compared with the slight implication of the spinothalamic tracts by the greater susceptibility of the phylogenetically younger posterior pathways. Kahn's explanation of this observation has already been cited.

GENERAL COMMENT

From the foregoing discussion, it is apparent that the effects of tumor of the cervical portion of the cord are protean and capricious. We have presented cases with normal spinal fluid findings, with normal neurologic findings and with a neurologic picture suggestive of amyotrophic lateral sclerosis or combined system disease. Other investigators have described a wide variety of clinical pictures produced by these tumors. Thus, the occurrence of mystagmus in 1 of his cases led Néri[13] to a diagnosis of multiple sclerosis. In a case described by Roussy and Levy[14] an exploration of the parietal lobe was erroneously carried out. Wechsler and Weinstein[15] described a case of

12. Friedman, E. D.: Compression of the Upper Cervical Cord in the Guise of Combined System Disease, Internat. Clin. **3**:103 (Sept.) 1941.

13. Néri, V.: La forme ataxique initiale des compressions medullaires cervicales, Rev. neurol. **1**:60 (Jan.) 1932.

14. Roussy, G., and Levy, G.: Existence d'une dissociation, dite corticale des troubles de la sensibilité par atteinte bulbo-protuberantielle et medullaire supérieure, Rev. neurol. **1**:145 (Feb.) 1930.

15. Wechsler, I. S., and Weinstein, E. A.: Dermoid Tumor in the Foramen Magnum with Astereognosis and Dissociated Sensory Loss, Arch. Neurol. & Psychiat. **44**:162 (July) 1940.

dermoid tumor in the foramen magnum which extended down to the second cervical vertebra and caused astereognosis and dissociated sensory loss in one upper limb. In addition, there were stiffness of the neck, vomiting, ataxia, diplopia, blurring of vision and vertigo. It is interesting to note, moreover, that the lumbar puncture showed no block and no elevation of the protein in spinal fluid. Eckel and Jacobs [16] described a case of chordoma of the upper cervical portion of the cord associated with headache, vomiting and papilledema. Wilson [17] mentioned the occurrence of paresis of the lower part of the face in a case of tumor of the cervical portion of the cord reported by Kraus and Silverman. He cited a similar observation by Elsberg. Involvement of sensation on the face with some loss of thermal and painful sense about the mouth may occur if the descending root of the fifth nerve is affected. Finally, it should be recalled that the neurologic syndrome accompanying platybasia, or basilar impression—a condition in which bony structures may impinge on the cervical portion of the cord as does tumor—is often highly suggestive of syringomyelia, multiple sclerosis or lateral sclerosis.

Several authors have commented on the variability of the sensory status in cases of tumor of the cervical portion of the spinal cord. Craig and Sheldon [5] noted definite loss of sensation in only 67 of the 91 cases reported by them, and of the cases in which loss of sensation was shown a level lesion was noted in only one-half. Soltz and Jervis [18] stressed that sensory levels, when present, often do not correspond to the site of the tumor. On the other hand, subjective sensory disturbances, notably pain or paresthesias, occur relatively frequently in the course of the history of these tumors. In the series of Craig and Sheldon, pain of so-called root type was present at some time in 93 per cent of the cases. These authors emphasized its occurrence, especially at night, when it may awaken the patient out of a sound sleep, causing him to sit up or walk about to gain relief.

Careful roentgenologic studies of the cervical portion of the spine may provide the only clue to the correct diagnosis, especially in cases in which the spinal fluid is normal. In rare instances in which the spinal fluid findings are normal and in which roentgenograms of the cervical portion of the spine are judged to be normal (as they were first erroneously reported to be in our second case) an exploratory lami-

16. Eckel, J. H., and Jacobs, W. F.: Malignant Spheno-Occipital Chordoma, J. Nerv. & Ment. Dis. **61**:471, 1925.

17. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940.

18. Soltz, S. E., and Jervis, G. A.: Extramedullary Tumors of the Upper Cervical Portion of the Spinal Cord, Bull. Neurol. Inst. New York **6**:274 (Aug.) 1937.

nectomy may be justified in order that the patient may be given the benefit of the doubt, even though the clinical picture is not entirely characteristic of an extramedullary tumor of the cervical portion of the cord.

SUMMARY

Seven cases presenting atypical features of extramedullary tumor of the cervical portion of the cord are described. In 2 cases the spinal fluid findings were normal; in 2 others the neurologic status was virtually normal; in 2 cases there was a clinical syndrome suggestive of amyotrophic lateral sclerosis, and in 1 case the clinical picture resembled that of posterolateral sclerosis. A brief review of other atypical cases reported in the literature is presented.

35 East Sixty-Fourth Street (21).

EFFECT OF GLUTAMIC ACID ON THE INTELLIGENCE OF PATIENTS WITH MONGOLISM

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THE PRESENT experiment constitutes a preliminary report on the effect of *l*(+)-glutamic acid on the mental function of persons with mongolism. The problem presents itself naturally, since the disease, as one of the most serious and least understood forms of mental deficiency, epitomizes the basic problem of the mechanism of intelligence. The distinct concomitant anatomic features of the mongolian idiot likewise underscore the psychosomatic relationship and essential unity of mind and body for medicine when it is inclined to relegate the problem of the mind to the more philosophic disciplines alone.

This intimate body-mind relationship was not overlooked by earlier investigators. In a classification of "idiots," J. Langdon Downs, in 1866, gave the first description of mongolism as a morbid entity. In the same year, Séguin,[1] although considering mongolism as a variant of cretinism, also gave a precise description of the condition. More recently, Benda[2] revealed his preoccupation with the same basic problem. He stated:

> Admitted that mongolism is a physical deviation which defaces the unlucky person stamped with this condition, why is mongolism of such serious importance that the child is doomed to idiocy or imbecility?

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From the Department of Neurology, Columbia University College of Physicians and Surgeons; the Service of Child Neurology, Vanderbilt Clinic, and the Neurological Institute of New York.

1. Séguin, É.: Idiocy and the Treatment by the Physiological Method, New York, W. Wood & Co., 1866.

2. Benda, C.: Mongolism and Cretinism, New York, Grune & Stratton, Inc., 1946.

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While our previous studies [3] on the effect of glutamic acid on intelligence did not include studies on mongolism, the results obtained have encouraged us to investigate its effect on this defect.

A measure of the magnitude of the problem of mongolism is apparent when it is realized that in all medical and psychologic literature the terms "mongolian idiot" (intelligence quotient 0 to 24) and "mongolian imbecile" (intelligence quotient 25 to 49) are used almost without exception to describe the mental development and lack of progress of children with mongolism. Whether or not one accepts these classifications without reservation, it is true that serious retardation in mental development characterizes the group with mongolism as a whole, and that the condition is one of the more serious forms of mental deficiency.

In a large group study, Brousseau [4] reported that in a series of 206 cases there were only 2 instances of mongolism, that of a girl with an intelligence quotient of 66 and that of a boy with a quotient of 54; these patients could be classified as morons or merely as feebleminded. On the other hand, 80, or 60.6 per cent, of the 132 boys with mongolism and 46, or 62.1 per cent, of the girls with the disease had intelligence quotients ranging from 25 to 49; thus 126, or 61.1 per cent, of the 206 children with mongolism belonged to the imbecile group. Fifty-one, or 38.6 per cent, of the boys with mongolism and 27, or 36.48 per cent, of the girls with mongolism had an intelligence quotient ranging from 7 to 25; thus, 78, or 37.8 per cent, of the 206 boys and girls with mongolism may be classified as idiots.

According to Benda,[2] "the mental age of an average group of mongoloid patients including all age groups ranges between 2 and 5 years." He cited the statement of Tennies [5] that "the majority of cases remain on a low imbecile level," and the observations of Wallin,[6] who reported on a large number of patients with a mental age ranging from 2 to 7.8 years. Benda [2] expressed the belief that of mentally retarded children "the mongoloid represents the clearest example of infantilism." Evidence from the literature in general reveals that most persons with mongolism fail to develop mentally at a normal rate and remain at a low psychologic level during their entire life span.

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3. Zimmerman, F. T.; Burgemeister, B. B., and Putnam, T. J.: The Effect of Glutamic Acid upon Mental Functioning in Children and Adolescents, Arch. Neurol. & Psychiat. **56**:489 (Nov.) 1946; A Group Study of the Effect of Glutamic Acid upon Mental Functioning in Children and Adolescents, Psychosom. Med. **9**:175 (May-June) 1947; The Ceiling Effect of Glutamic Acid upon Intelligence in Children and Adolescents, Am. J. Psychiat. **104**:593 (April) 1948.

4. Brousseau, K.: Mongolism, Baltimore, Williams & Wilkins Company, 1928.

5. Tennies, L. G.: Some Comments on the Mongol, Am. J. Ment. Deficiency **48**:46, 1943.

6. Wallin, J. E.: Mongolism Among School Children, Am. J. Orthopsychiat. **14**:14, 1944.

MATERIALS AND METHODS

Choice of Patients.—Because of the encouraging results we obtained in treating mentally defective patients with *l* (+)-glutamic acid, we decided to test the effect of this substance on the most challenging type of mental deficiency—mongolism. The patients in this study form only a fraction of a large group of persons with mongolism now receiving glutamic acid, but results so far obtained seem to justify a preliminary report. The large group consists of infants, children and adolescents, and the classic diagnostic criteria of mongolism for each group were used in the selection of cases. The present paper is a report on our first 7 patients to complete six months of glutamic acid therapy. Four of the group were boys and 3 were girls, their ages ranging from 3 years 6 months to 14 years 1 month at the time of the initial test.

Dosage.—As emphasized in our previous reports,[3] there is no relation between the age of the patient and the effective dose. The proper dose must be worked out empirically for each individual case and depends on the simultaneous utilization of psychologic, neurologic and psychiatric data.

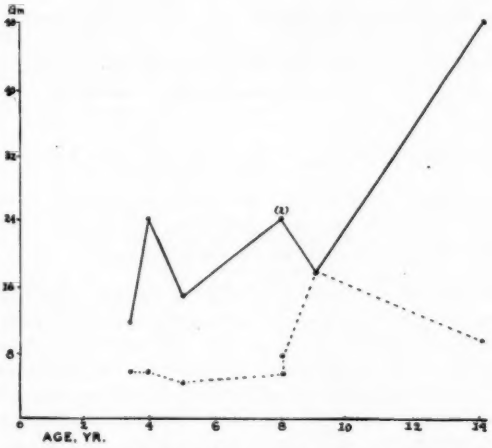

Chart 1.—Dosage of glutamic acid in treatment of children with mongolism. Values for the first effective dose are indicated by the line of dots; values for the maximum effective dose, by the solid line.

Chart 1 illustrates this point. Patients 3 and 5 have the same chronologic age (8 years old), and each required 24 Gm. of glutamic acid daily to produce the maximum effect, while patient 4, who is one-half their age (4 years old) likewise required a maximum effective dose of 24 Gm. While the curve does show a slight positive mathematical increment in relation to age and dose, as illustrated by a required dose of 12 Gm. for patient 1 (3½ years old) and 48 Gm. for patient 7 (14 years old), this relation is not sufficient for an accurate estimation of dosage.

The fallacy of citing an average dose when the average represents the central tendency of a large sigma has likewise been brought home to us. Some physicians have seized on this average, forgetting that an average of widely scattered doses has little therapeutic validity.

Glutamic acid acts by increasing the capacity to learn. In arriving at the correct dose, it is necessary to continue a particular dose long enough to determine the degree of increased capacity and to what extent this particular dose stimulates maximum mental functioning for the individual patient.

Since the element of time enters into learning regardless of increased capacity, treatment must be supervised carefully until the ceiling effect is reached.

Procedure.—Prior to glutamic acid therapy, each child was given a Stanford-Binet intelligence test (Form L, 1937 Revision) [7] and a Merrill-Palmer performance test.[8]. The battery of tests was repeated at the end of a six month treatment period. Table 1 shows the chronologic age, the Stanford-Binet mental age and the intelligence quotient for each of the 7 children at the beginning of our experiment.

As may be observed in table 1, our children with mongolism ranged in age from 3 years 6 months to 14 years 1 month, the average chronologic age for the group being 7 years 4 months at the time of the initial test. Their mental ages at that time ranged from 2 years 7 months to 4 years 10 months, with an

TABLE 1.—*Chronologic Age, Mental Age and Stanford-Binet Intelligence Quotient Prior to Glutamic Acid Therapy*

Case No.	Chronologic Age		Mental Age		Intelligence Quotient
	Yr.	Mo.	Yr.	Mo.	
1	3	6	2	7	74
2	9	5	2	10	30
3	7	11	4	2	53
4	4	1	2	8	65
5	7	11	4	4	55
6	5	5	2	9	51
7	14	1	4	10	35

average mental age for the group of 3 years 6 months. The scatter of intelligence quotients (ratio of mental age to chronologic age) is from 30 to 74, with 4 of the 7 children rating between 50 and 65. This gives an average intelligence quotient of 51.86 for the group at the beginning of the experimental period, a value which is considered low enough to indicate serious retardation. It falls well within the classification of "defective" intelligence (intelligence quotient below 65) and reflects very slow mental development. As a group, however, our sample of children with mongolism rated higher mentally on the initial test than did the majority of patients reported by most investigators, a finding which is, no doubt, based to a large extent on age, inasmuch as all but 2 of our children were under 9 years of age at the beginning of the treatment period. One might expect lower intelligence quotients if the children had been older, since the discrepancy between mental age and chronologic age usually becomes greater with increase in chronologic age and results in a lowered ratio between the two ages, i. e., in a lowered intelligence quotient. This tendency for the intelligence quotient to drop as age increases is, of course, typical of seriously retarded children in general, and is not limited to mongolism.

7. Terman, L. M., and Merrill, A.: Measuring Intelligence, Boston, Houghton Mifflin Company, 1937.

8. Stutsman, R.: Mental Measurement of Preschool Children, Yonkers-on-Hudson, World Book Company, 1931.

It seems worth while in this connection to point out that in estimating intellectual level, group averages are often erroneously applied to all members of a group, with the result that differences in capacity are obscured and the ability of some persons who rate above the group mean is underestimated. Our sampling of children with mongolism shows clearly (table 1) that it is incorrect to classify all such children as "idiots" or "imbeciles," especially the younger ones. Only 2 of our 7 children fell within the imbecile range at the time of the initial test.

Table 2 gives the performance test scores of our children with mongolism prior to treatment, the ratings ranging from 2 years 2 months to 6 years 3 months, with an average score for the group of 3 years 5 months. This group mean approximates the average obtained on verbal material, suggesting serious

TABLE 2.—*Merrill-Palmer Test Scores Prior to Glutamic Acid Therapy*

Case No.	Performance Score		Performance Quotient
	Yr.	Mo.	
1	2	7	74
2	2	2	23
3	4	2	53
4	2	3	55
5	4	0	51
6	2	7	48
7	6	3	45

TABLE 3.—*Intelligence Test and Retest Scores Before and After Six Months of Glutamic Acid Treatment*

Case No.	Mental Age				Intelligence Quotient		
	Test 1		Test 2				
	Yr.	Mo.	Yr.	Mo.	Test 1	Test 2	Point Change
1	2	7	3	9	74	94	20
2	2	10	3	6	30	35	5
3	4	2	4	9	53	56	3
4	2	8	3	2	65	69	4
5	4	4	4	9	55	56	1
6	2	9	3	4	51	56	5
7	4	10	5	9	35	41	6

retardation also in the nonlanguage type of test, in which motor coordination is involved to a greater extent. In terms of ratio of mental age to chronologic age, a scatter of performance quotients was obtained which ranged from 23 to 74, with a group mean of 49.85 points. The latter is at the upper end of the "imbecile" level and slightly lower than the verbal quotient of 51.86.

Our children with mongolism prior to glutamic acid treatment thus showed a rate of development on both verbal and motor tests which was slightly higher than that expected of children one-half their age. In other words, mental growth in this group up to the time of experimentation had been progressing at only one-half the speed attained by children having average intelligence.

RESULTS

Individual intelligence quotients with the Stanford-Binet intelligence test before and after six months of glutamic acid treatment appear in table 3, as well as point changes in the intelligence quotient.

All 7 of the children with mongolism showed some rise in the intelligence quotient after glutamic acid treatment, as may be observed in table 3, the increments ranging from 1 to 20 points. As a group, the average point gain was 6.28, raising the mean intelligence quotient from 51.86 to 58.14. This gain agrees well with results obtained from a group of 38 of our most seriously retarded children without mongolism, reported on previously,[4] in which the average increase in intelligence quotient was 6.31 points during the first six months of glutamic acid therapy. In chart 2 individual point changes in intelligence quotient are presented graphically.

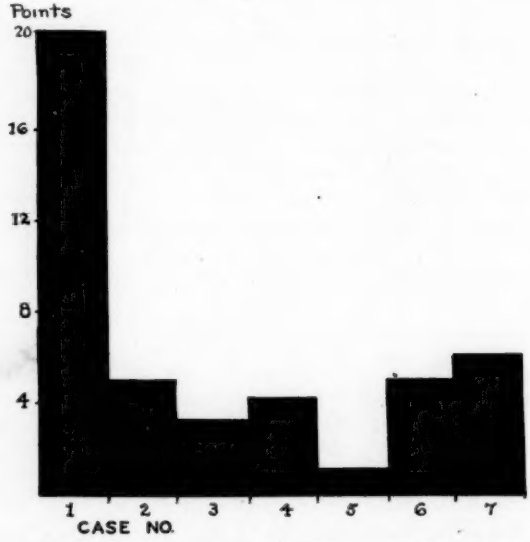

Chart 2.—Individual point changes in intelligence quotient following six months of treatment with glutamic acid.

The average mental age of our present group of children with mongolism was raised from 3 years 6 months to 4 years 2 months, or a gain of 8 months in the six month treatment period. This is higher than the rate of growth expected of children having average intelligence (6 months in a six month period) and more than twice that of the previous rate of mental development of the group with mongolism. It is slower, however, than that reported for the group of most seriously retarded children without mongolism, which was 12 months during the first six months of treatment.

Because patient 1 showed a remarkable gain of 20 points, in contrast to that made by each of the other 6 children (table 1), data have also been analyzed with those for patient 1 omitted. Our sample is so small that it is believed that such a radical change in intelligence quotient as patient 1 revealed may prove atypical of our larger group of patients with mongolism.

Results for patients 2 to 7, inclusive, show an average rise in intelligence quotient of 4.00 points after the first six months of treatment and a gain in mental age of 6.6 months. These findings suggest an increase in development which is slower than that obtained from our seriously retarded group of children without mongolism, but one which approximates that of children having average intelligence. It represents a rate of development during treatment which is twice that reached by the group of 6 children with mongolism prior to the experimental period.

TABLE 4.—*Merrill-Palmer Tests and Retests Before and After Six Months of Glutamic Acid Treatment*

Case No.	Performance				Performance Quotient		Point Change	
	Test 1		Test 2					
	Yr.	Mo.	Yr.	Mo.	Test 1	Test 2	Plus	Minus
1	2	7	2	8	74	67	..	7
2	2	2	2	10	23	28	5	..
3	4	2	4	2	53	50	..	3
4	2	3	3	2	55	69	14	..
5	4	0	4	2	51	50	..	1
6	2	7	2	7	48	44	..	4
7	6	3	6	6	45	46	1	..

Even when the data for patient 1 are omitted and the more conservative figure is accepted, a positive trend is indicated, and our results suggest that, under the conditions of our experiment, glutamic acid definitely facilitates mental functioning in our children with mongolism, acceleration being reflected in a rise of retest intelligence quotients. Results of the Merrill-Palmer tests and retests are presented in table 4.

In contrast to the gains made on verbal material after six months of glutamic acid treatment, our group with mongolism did not show striking improvement on the nonlanguage type of test. The group performance score was raised only 3 months, from 3 years 5 months to 3 years 8 months, and the performance test quotient, from 49.85 to 50.59. Although retest performance scores did not reflect any losses during treatment, sufficient gain was not made in 4 of the 7 cases to prevent a lowering of the performance retest quotients. These changes in performance test quotients are shown graphically in chart 3. As a

group, approximately the same rate of growth was maintained on motor tests during treatment as that previously recorded, namely, 3 months in a six month period.

These results on the performance tests are also very different from those reported for our group of seriously retarded children without mongolism, in which an average gain of 9 months in performance retest scores during the first six months of glutamic acid therapy occurred. It is true, however, that the group without mongolism showed more rapid gains during the second six months of glutamic

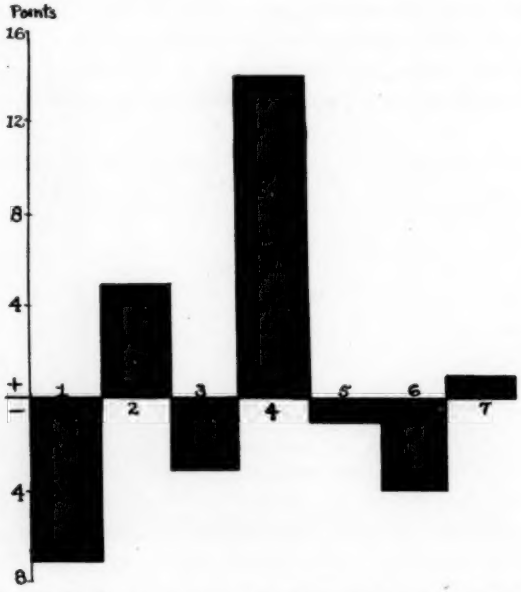

Chart 3.—Individual point changes in performance quotient after six months of treatment with glutamic acid. Numbers on horizontal line indicate case numbers.

acid therapy on performance tests than on verbal material. Our sample of children with mongolism, therefore, may improve somewhat on motor tasks under continued treatment, but it is believed that the findings to date suggest that a real difference may exist in the potential response of these two types of mental deficiency to glutamic acid treatment, it being much more difficult to accelerate the group with mongolism in the motor field.

During both test sessions, more awkwardness in manipulating objects and form board material was apparent among our children with

mongolism than among the defective group without mongolism. It is likely that failure of the group with mongolism to improve on performance tests during the initial phase of treatment may be dependent largely on physiologic or constitutional factors related to motor ability, rather than to psychologic components in the perceptual field.

SUMMARY AND COMMENT

On verbal intelligence tests our group of children with mongolism showed a gain in mental age after six months of glutamic acid treatment which was equivalent to that of children having average intelligence. This gain represented an increase in rate of development which was twice as great as that formerly achieved. Gains were somewhat lower, however, than those reported in a group of children with undifferentiated mental deficiency. Although our sample of children with mongolism is small, a positive trend is definitely indicated, suggesting that glutamic acid facilitates mental functioning in this form of mental deficiency also, acceleration being reflected in an increase of retest intelligence quotients.

Similar gains were not apparent on performance tests during the initial stage of treatment. In a group of defective children (without mongolism) they were secured, although they were less striking than increases on verbal material. During the second six months of treatment, however, performance retest scores increased more than verbal quotients in the group without mongolism. Our present sample of children with mongolism, therefore, may show some gain on motor tests under continued treatment, but it is believed that results with mongolism to date point to a genuine difference in potential response to glutamic acid therapy, and that physiologic rather than psychologic factors make it difficult for children with this defect to improve their performance on motor tasks.

The pathologic changes in the cord described by Benda [2] may throw light on the indifferent motor response to glutamic acid therapy in patients with mongolism. In a study of the spinal cords of 12 cases of mongolism, this investigator found a characteristic pathologic picture, ranging from hypoplasia to true fetalism and arrest of development with pathologic differentiation. No normal cords were found, and the pathologic alterations noted were not observed in any case of a large control material of other types of mental deficiency. The pathologic features included insufficient myelination, spongy edema of the white matter, vascular stasis and insufficient myelination of the peripheral nerves. The most unique developmental defect was an abnormal persistence of the roof plate with junction of the column of Clarke.

The type and degree of pathologic involvement of the cord observed would appear to be ample to explain impairment of the coordination of muscular activity. The uniform defect in the column of Clarke (nucleus dorsalis) itself would seem to contribute substantially to the impairment of coordinated movement by interruption of the dorsal spinocerebellar fibers running to the cerebellum.

As stated in previous communications, the rationale for the use of *l*(+)-glutamic acid in the treatment of defective mental function is based on a number of experiments which indicate a particular relation to cerebral metabolism. Weil-Malherbe [9] reported that *l*(+)-glutamic acid is the only amino acid metabolized by the brain. The experiments of Nachmansohn and his associates,[10] likewise, indicated that the electrical changes during nerve activity are intrinsically connected with the release of acetylcholine. The latter substance is synthesized by an enzyme, choline acetylase.[11] Nachmansohn found that *l*(+)-glutamic acid [12] has a catalyzing effect on the rate of production of choline acetylase. According to in vitro experiments, then, glutamic acid acts as a catalyst, or stimulant, in a complex enzyme chain reaction necessary for the production of the electrical nerve impulse.

Since learning depends on the transmission of sensations from the environment through the nerve impulses to be integrated into a state of conscious awareness, it would appear that intelligence depends basically on the degree of conscious awareness. Glutamic acid would act, then, by increasing the degree of conscious awareness, thus facilitating the learning process. When emphasis is shifted to the capacity of a person to learn, the concept of intelligence breaks the bonds of static definition and opens the way to an understanding of the phenomeon on a sound physiologic level.

The present results in the verbal tests, although tentative, because of the smallness of this group of patients with mongolism, reveal, nevertheless, a trend similar to our findings in the treatment of undifferentiated mental retardation with glutamic acid. This offers further evidence for a basic physiologic mechanism underlying the learning

9. Weil-Malherbe, H.: Studies on Brain Metabolism: Mechanism of Glutamic Acid in Brain, Biochem. J. **30**:665, 1936.

10. Nachmansohn, D.; Cox, R. T.; Coates, C. W., and Machado, A. L.: Action Potential and Enzyme Activity in the Electric Organ of Electrophorous Electricus: II. Phosphocreatine as Energy Source of the Action Potential, J. Neurophysiol. **6**:383, 1943.

11. Nachmansohn, R., and Machado, A. L.: The Formation of Acetylcholine; A New Enzyme: Choline Acetylase, J. Neurophysiol. **6**:397, 1943.

12. Nachmansohn, D.; John, H. M., and Waelsch, H.: Effect of Glutamic Acid on the Formation of Acetylcholine, J. Biol. Chem. **150**:485, 1943.

process, at the same time indicating that the amount of potential mental improvement depends on the relative intactness of the organic substrate of the mind.

APPENDIX

While this study is primarily objective, the clinical records reveal a close relation to the quantitative findings, and are accordingly appended.

CASE 1.—A girl aged 3½ years, the second child of two siblings, had a normal birth. She sat up alone at 10 months, walked alone at 22 months and said "mamma" at 15 months. When first seen she was able to say only "mamma," "bye-bye" and "gagga" (for "daddy"). She was jealous of her older sister, cried when the latter entered the room and bit and scratched her at every opportunity. She did not play well with other children unless they were younger than herself and there was no interference.

Observation and physical examination revealed a characteristic picture of mongolism. After a psychometric examination she was given 2 Gm. of *l* (+) = glutamic acid three times a day. One month later her mother reported that she now played better by herself and exhibited more sustained interest in her toys. "Instead of looking at the toy and throwing it away, she now plays with it ten minutes or longer." Four new words, "apple," "head," "ball" and "cow" were added to her vocabulary. She was still jealous of her sister but at a recent party played with her over an hour, an event which the mother considered something of a minor miracle. After the dose was increased to 3 Gm. three times a day, the family reported that she was "beginning to say lots of words, was more observant and much keener."

Ten days after the dose was increased to 18 Gm. per day, insomnia developed; she climbed out of bed, over the side boards, in the dark and went to sleep with her sister.

After her optimum dose of 12 Gm. per day was arrived at, she slept soundly at night and continued her steady improvement. She walked up to people and smiled and answered them when spoken to, instead of hanging her head shyly, and was generally more outgoing. Her facial expression was much brighter, and she appeared more alert. Her vocabulary continued to increase, and temper tantrums were less in evidence. The mother reported further that relatives and neighbors who knew nothing about the treatment exclaimed over her improvement.

CASE 2.—A Negro boy aged 9 years had the characteristic features of mongolism. Birth had been normal. He sat up at 1 year and walked at 3 years of age. He formed sentences at 5 years of age.

Aftr a psychometric examination, he was given 18 Gm. of glutamic acid daily, and after two weeks of medication he experienced gastric upset. Medication was discontinued for a week; smaller doses were then instituted and were gradually increased to the original 18 Gm., an amount which was continued through the six months of treatment. First evidences of improvement were noted by the mother six weeks after the beginning of treatment. She stated, "He notices things more, and will even mind me and go and turn off the radio when I ask him." Later the boy's father reported that on one occasion he forgot to remove his keys from his parked car. The patient spontaneously brought them to him, instead of his usual custom of "throwing them away." On another occasion, when his mother lost 50 cents and was looking for it, the patient reminded her that she had placed it in her purse. His teacher gave him an "A" in conduct and called up his mother and wanted to know what she was "doing

for him." Other people who knew nothing of the treatment told his mother that he was "different and behaving much better." Miss K., a member of the mental hygiene group in the patient's community, came to the hospital for a personal interview and said there was a "tremendous improvement—he was more cooperative, quieter, and his conversation was more to the point."

CASE 3.—A girl aged 8 years had a birth complicated by placenta previa. She sat up at 7 months, walked at 2 years and said words at 3 years of age. The mother reported that she was well behaved and presented no disciplinary problem. The diagnosis of mongolism was first made by a pediatrician after a psychologist, who was testing the child, had suggested its possibility. After physical, neurologic and psychometric examinations, the child was given an initial dose of 8 Gm. of glutamic acid daily.

One month later the mother noted that the patient could print her name better and that she recognized several colors, instead of the two colors learned before treatment. She was likewise quieter in her behavior. Previously, she used to come to her father's bed in the morning and kick him in the back roughly. "Now she gets into bed and lies there quietly." After the dose of glutamic acid was increased to 18 Gm. per day, she became more active physically, "talked a lot more" and "had more pep." She lost her previous dull facial expression and appeared bright and alert.

When the optimum dose of 24 Gm. per day was established, she showed a spurt in improvement. She used many more words and was much more alert. Her mother reported that on one occasion she backed her father's car out of the garage on the battery in order to have enough room to get her swing out.

CASE 4.—A girl aged 4 years had the characteristic features and stigmas of mongolism. After physical, neurologic and psychologic examination, she was given an initial dose of 6 Gm. of glutamic acid a day. No improvement was noted until the dose had been increased to 18 Gm. per day for a period of two months. The mother then reported a spurt in improvement. The child learned to call her playmates by their first name, lost her timidity and sought out other children to play with them. When an optimum dose of 24 Gm. per day was established, she used many new words and appeared brighter and more alert.

CASE 5.—The mother had been confined to her bed during the last trimester of pregnancy, after an automobile accident. The child sat up at 16 months, stood with assistance at 2 years and walked alone at 3 years of age. He said his first words at the age of 4 years but was unable to form complete sentences at the age of 8, at the time he first appeared for treatment. His mother complained of his behavior, saying he did not obey her and that he "sat down on the floor like a mule and had a cruel streak." He frequently attempted to push his fingers down the throats of other children.

After physical, neurologic and psychometric examination, an initial dose of 6 Gm. of glutamic acid per day was given. One month later his vocabulary was reported to be increased, and he appeared more alert. His mother reported that he concentrated more on what people were saying. "Before when people talked, he often paid no attention and would stare out the window and watch the cars pass."

With an eventual optimum dose of 24 Gm. per day, he "behaved more politely" and was "much easier to manage at home."

CASE 6.—A boy aged 5 years had the characteristic physical characteristics of mongolism. He sat up at 1 year, stood up at 1½ years and walked at 2 years of age. He said his first words at 2 years of age and formed sentences at the age of 4.

After appropriate physical and psychologic examination, he was given an initial dose of 6 Gm. of glutamic acid. With an eventual optimum dose of 15 Gm. per day, his mother reported that he occupied himself more and "played for a longer time at any one thing than ever before." He became more sociable and suggested games with other children. He expressed himself better and used longer sentences. He learned to undress himself rapidly and well, whereas before he had done it clumsily. He was also much more active physically, noticed things more and appeared more alert.

CASE 7.—A boy 14 years old had physical characteristics of mild mongolism. The history revealed the usual retardation in development. After appropriate physical and psychologic examination, glutamic acid therapy was instituted. From an initial dose of 9 Gm. per day, an eventual optimum dose of 48 Gm. per day was established. Improvement was slow but steady. He used words better and employed new words in a correct sense. He began to carry on a conversation over the telephone when he answered it, instead of saying the usual "yes" or "no." He was quieter in his behavior and applied himself to his home work for longer periods. His school work was neater and more orderly. He took more part in games and was not so timid in playing with other boys in the park. His gait showed better coordination, and he appeared brighter and more alert.

416 North Bedford Drive.

ABSENCE OF SPASM DURING ONSET OF PARALYSIS IN ACUTE ANTERIOR POLIOMYELITIS

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THE CLINICAL signs and symptoms of acute anterior poliomyelitis have been well documented in the literature by eminent and capable neurologists. The studies leading to such reports were conducted for the most part prior to 1918.

As the consequence of a focusing of interest on the residual effects of the disease, its study and treatment became concentrated among pediatricians and orthopedic surgeons. In recent years, as the result of exclusion of neurologists from active participation in continued study of the disease, we believe that a number of misconceptions concerning the symptomatology, pathology and pathophysiology have developed. This has, in turn, led to research which we believe is unrelated to the disease. Interest in such studies has been awakened by the conception that "paralysis is unfortunately a feature of this disease, but paralysis proves after all to be a minor consideration in most cases of infantile paralysis. Muscle spasm, mental alienation and incoordination are far more damaging to bodily mechanisms." [1] In order that one may discuss muscular spasm intelligently, it is necessary that the term be defined and its meaning understood. The term "muscular spasm" as understood by neurologists is applied to a state in which there is sustained involuntary tetanic contraction of muscle. This contraction is reversible. It may be caused by a number of different conditions and may appear in various disorders and injuries of the nervous system. It may occur from changes in the peripheral nervous system, as in carpopedal spasm, the result of a breakdown of accommodation in a nerve, with production of repetitious stimuli; such a disturbance may follow pressure

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1. Pohl, J. F., and Kenny, E.: The Kenny Concept of Infantile Paralysis and Its Treatment, Minneapolis, Bruce Publishing Company, 1943.

block of a nerve, hyperventilation or parathyroid deprivation. Muscular spasm may be seen as a visceromotor reflex evoked by pain. More familiar is that form which results from injury or disease of the central nervous system. Here it is an expression of diminished inhibition leading to an increase of reflexes, such as the stretch reflex and the reflexes evoked by nociceptive stimuli. If, therefore, in anterior poliomyelitis one is concerned with a form of muscle spasm which suggests the study of a possible interruption of inhibitory impulses, perhaps in internuncial pathways, it is necessary that there be good clinical evidence that such a type of muscular spasm exists.

The muscular spasm observed by the adherents of a recent misconception is something quite foreign to the experience of neurologists. For example, among its definitions is one which states that one type of muscular hypertonus may be illustrated by the so-called foot drop, which should more accurately be named "foot retraction." [2] In general, it may be described thus:

> . . . characterized by shortening of the skeletal muscles which appears in the acute stage of the disease and may persist for months or years. It may be identified in the early stages by characteristic deformities, by prominence of tendons, by flatness and narrowing of muscle bellies, by increase or decrease in the number and depth of skin folds or creases, by limitation of range of motion and by other evidence of muscle shortening. The muscles in spasm are painful to stretch or pressure and may often be weak or even completely paralyzed.

Moreover, in describing a so-called hyperirritable stretch reflex (another form of muscular spasm), it is stated:

> There is a limitation of the range of passive motion which is variable in degree. There is no resistance to passive stretch of the involved muscle until the point of limitation of motion is approached, when further passive motion becomes impossible due to resistance of the strongly contracted, painful muscle. . . . Since there is no resistance to passive stretch through a certain range of motion, this phenomenon differs from the rigidity in Parkinson's disease and the spasticity in hemiplegia.

To a neurologist, this picture certainly does not reflect that of a muscular spasm.

Because of the various recent reports of the widespread presence of muscular spasm in anterior poliomyelitis previously detected by the clinical signs here noted, a number of investigators have studied the action potentials of the muscles in this disease. Having found action potentials in muscles at rest in the later stage of the disease, some, among whom are Bouman and Schwartz,[3] have come to the

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2. Kabat, H., and Knapp, M. E.: Mechanism of Muscle Spasm in Poliomyelitis, J. Pediat. **24**:123-137 (Feb.) 1944.

3. Bouman, H. H., and Schwartz, R. P.: Degree, Extent, and Mechanism of Muscle Spasm in Infantile Paralysis, New York State J. Med. **44**:147-153 (Jan. 15) 1944.

remarkable conclusion that these are the result of muscular spasms which cannot be demonstrated clinically; thus, they say:

> . . . It is also clear that the clinical observance of a resistance to stretch which is greater than that of a normal muscle will in most cases be difficult. Not only will it be hard to estimate quantitatively the degree of such resistance; it is also quite possible that a muscle can contract without any visible movement. It is reasonable to assume that a reflex contraction on stretching a muscle might be too weak to be observed clinically.

However, others, Watkins [4] for example, have more reasonably called attention to an increase in irritability to stretching of muscles during the acute stage, without any correlation to clinical evidence of spasm, tenderness or pain on stretching. The pattern of electrical discharges produced by stretching resembled in appearance that obtained from muscles in a state of tonic contracture or spasm secondary to fracture of an extremity.

Another type of hyperirritability was found later when action potentials were obtained from muscles at rest. This he compared with the pattern found in cases of progressive muscular atrophy and that obtained from muscles during regeneration of nerves. He also found some potentials which he claimed resembled those occurring with upper motor neuron lesions.

In this paper, we shall not discuss the meaning of changes in electrical potentials of muscle. It is desirable, however, to point out that the cause of many of the changes—spontaneous discharges of resting muscles, isochronism and response to stretch—is unknown. It is unwise at this time to identify muscular spasm by means of electromyography alone.

It is also desirable to point out that in different epidemics there has occurred a difference in distribution of lesions in the nervous system—in some there were many lesions in the corticospinal pathways; in others, in the peripheral nerves; in others, in the cerebellum and the brain stem. It should not surprise one at times to find evidence of an upper motor neuron lesion. Thus, Weisenburg [5] stated that frequently the limbs were found to be rigid and the reflexes prompt and that it was not unusual to obtain the ankle clonus and the Babinski phenomenon. He stated that whenever in a paralyzed limb there were hypertonicity and ankle clonus or the Babinski sign was elicited, these signs were

4. Watkins, A. L.: Electromyographic Studies in Poliomyelitis, Journal-Lancet **64**:233-236 (July) 1944.

5. Weisenburg, T. H.: Poliomyelitis Epidemic in Philadelphia, 1916, M. Clin. North America **1**:393 (Sept.) 1917.

nearly always the result of a meningeal complication and an increase of cerebrospinal fluid, for almost invariably with lumbar puncture these phenomena disappeared.

Whether or not his explanation was correct, in the particular epidemic described evidence of an upper neuron lesion was found. On the other hand, in a number of other epidemics such findings were rare indeed. This variability may explain why in some epidemics (Wickman) the widespread occurrence of tenderness and pain led to the concept of a polyneuritic type of poliomyelitis and in other epidemics, such as the one reported by Weisenburg, pain and tenderness were relatively rare. An analysis of the literature on recent concepts of the disease leads to the conclusion that in the early hours of paralysis, except for meningeal signs, the clinical evidence of muscular spasm is largely that of limitation of motion and pain when a muscle is stretched. There is nothing new in this observation. In 1914, Fraser described the pain produced when tendons or capsular structures were stretched by passive movements. During the acute stage pain occurred frequently in limbs that at no time showed paralysis; on the other hand, pain could be elicited in limbs that were totally paralyzed. After the acute stage was passed, the capsular structures, tendons and muscles appeared to stiffen. The tenderness was usually localized more particularly to the region of joints and occurred in joints controlled by muscles which were completely flaccid, as well as in joints where the muscles were only partially affected, and it simulated the joint pain of arthritis, without local points of tenderness on pressure. Properly, we believe, Fraser attributed the pain to changes in joints, tendons and muscles, and not to a lesion of the upper motor neuron.

Although every neurologist is familiar with the evolution of the signs and symptoms during early anterior poliomyelitis, it was felt that a careful study of such changes as could be related to the presence or absence of muscular spasm or tenderness or stretch pain was warranted in order that these signs might be redescribed in the light of the recent misconceptions.

It is generally accepted that the total damage to the nervous system occurs during a relatively short period following the invasion of the nervous system by the virus of acute anterior poliomyelitis. The sequelae of this damage later develop in the form of such changes as alterations in growth, contractures, deformities and vascular changes. The reports on symptoms and treatment during the so-called acute stage do not clearly define the limits of this stage, and for the most part do not reflect the early changes during the first several hundred hours following appearance of the first symptoms of the disease. In

part, this is due to the fact that orthopedic surgeons defined the termination of the acute stage as that time when tenderness had disappeared. In part, the reason is found in the fact that examinations and treatment during these very early hours were unavailable because of conditions brought about by necessity of quarantine. It was felt desirable, therefore, again to ascertain whether muscular spasm occurred during the development of paralysis, whether it was in any way related to paralysis and whether there was any muscular tenderness or any pain consequent to stretching of muscles during the same time.

PRESENT INVESTIGATION

Plan of Study.—Eleven neurologists were rotated in tours of duty day and night for thirty days in the Municipal Contagious Disease Hospital. Frequent examinations of 32 muscle groups of each patient were made from the time of his entrance to the hospital after the diagnosis or presumptive diagnosis of acute anterior poliomyelitis. As can readily be seen, this program resulted in the examination of a pool of patients, consisting at first of the few who were admitted on the first day and increasing with subsequent admissions. During the period of thirty days the pool was diminished by the discharge of patients at the end of their estimated period of quarantine to other hospitals or to their homes. From the pool there were also removed such patients as may have died or in whom a predominantly bulbar type of paralysis developed.

After exclusion of such cases as those in which death or respirator life afforded a relatively short period of observation, we had available 30 cases for periods of study of sufficient length to permit of an analysis.

These cases were divided into two groups. In the first group, of 16 cases, the paralysis developed to a degree which could be graded as 0, 1 or 2, 0 indicating total paralysis; 1, a flicker of movement, and 2, a slight movement against gravity. In the second group, of 14 cases, the muscles were either normal, as indicated by 5, or weak, as indicated by 4.

Many signs and symptoms were recorded, such as the abnormal reflexes, rigidity of the neck, the Brudzinski sign, the spine sign, the Ruhrah-Hoyne sign, direct myotatic irritability, tremors and fasciculation.

For the purpose of this report, only muscular spasm, muscular tenderness and pain elicited by stretching a muscle were analyzed. Muscular spasm was interpreted by the accepted neurologic definition of a sustained, reversible tetanic contraction of a muscle or, to a lesser degree, of resistance of a muscle to pressure. The types of muscular spasm ordinarily attributed to meningeal reaction common to all types of inflammatory diseases of the brain and cord, such as rigidity of the neck and spine and the Kernig and Brudzinski signs, were not considered. Tenderness was sought for by pressure on the muscle or by tapping the muscle with a reflex hammer. In the study of pain produced by stretching a muscle, the stretching was both rapid and slow. Pain as a result of stretching a muscle occurred only after the muscle had been stretched most of its potential stretch distance, and only in the last period, when the muscle might be stretched a distance usually not exceeding 1 inch (2.5 cm.).

This type of stretch pain differed in no way from that which we had observed in experimentally produced section and suture of the sciatic nerve in the cat (report to Office of Scientific Research and Development). In this case

it began when a sufficient time had elapsed after suture to permit either the development of overlap of sensation or recovery. From the muscle groups examined for stretch pain were excluded such groups as could not adequately be stretched—for example, the abductors of the arm. There remained 16 potential muscle groups on each side, or a total of 32 muscle groups. In this part of the analysis were included only such muscle groups as those in which the last examination was recorded as 0, 1 or 2. Therefore, in some cases all the 32 muscle groups were included; in some perhaps only 7 groups were studied.

In the total series of 30 cases, 670 muscle groups were examined. These were examined a variable number of times, depending on the length of the patient's residence; the total number of examination of muscle groups was 9,144; the number for the group with significant paralysis, 3,192, and that for the other (unparalyzed) groups, 5,952.. There was a total of 222 muscle groups in the former and of 448 in the latter, in which there were 186 examinations of 32 muscle groups. The time constant of the examinations was compared with the first sign or symptom which indicated the beginning of the disease. The decision to time the examination in this way was prompted by our inability accurately to determine the time of invasion of the nervous system. In the first group the successive times ranged from 6 to 197 hours, with a median of 106 hours. In the second group, the times ranged from 3 to 300 hours, with a median of 94 hours.

Analysis of Data.—It may at once be said that in no case, even when a number of cases not included in this special analysis were included, was there any indication of muscular spasm.

In analysis of data for the first group, in which the resulting paralysis was severe, the terminal time was held at 200 hours after onset. Up to the two hundreth hour the total number of examinations of muscle groups was 2,919. Of this entire number, muscular tenderness was recorded in 236 instances, or 8 per cent. The first instance of such tenderness was noted 43 to 48 hours after onset. Early during the period of study there occurred a case in which 9 muscle groups remained tender from a period of 61 or 66 hours to one of 97 or 102 hours. In the other cases, tenderness occurred only in scattered muscle groups and infrequently, until it appeared again in 2 cases, in which it continued until the two hundredth hour. Except for these 3 cases, the sign was rare. When tenderness was present, it occurred in 6 unaffected muscle groups, in 3 groups graded 4, in 13 groups graded 3, in 8 groups graded 2, in 15 groups graded 1, and in 191 totally paralyzed muscle groups.

Stretch pain was found first in 1 muscle group during the period of 67 to 72 hours after onset, then it occurred in 9 successive examinations of 9 muscles in 1 case; it was then seen in only 5 of 1,211 examinations of muscle groups until the period of 146 to 150 hours after onset, when it was observed in 12 of 103 muscle groups, and from then until the two hundredth hour it was found in 43 of 577 examinations of muscle groups.

It occurred in 2 unweakened muscle groups, in 5 muscle groups graded 4, in 1 each of muscle groups graded 2 and 3, respectively, in

3 muscle groups graded 1 and in 70 completely paralyzed muscle groups. Of 2,653 examinations of muscle groups during the 200 hours following the first symptom, stretch pain occurred in only 82 cases, or 3 per cent. In 9 of the 16 cases it was never observed.

From figure 1, one can visualize the evolution of tenderness and stretch pain as related to the amount of paralysis which was developing. It may be seen that, except for the particular loading of a single case in which 9 muscle groups showed tenderness, with stretch pain a bit

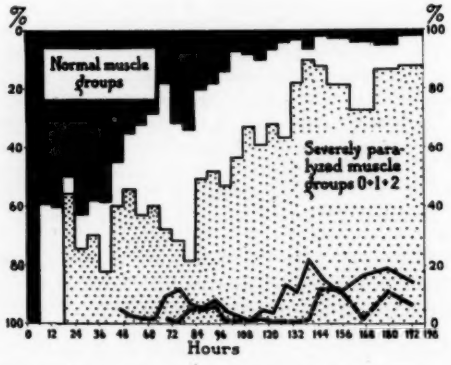

Fig. 1.—Histogram illustrating the evolution of paralysis and of tenderness and stretch pain. The heavy black line shows the percentage of muscle groups with tenderness; the double broken line, the percentage of muscle groups with stretch pain.

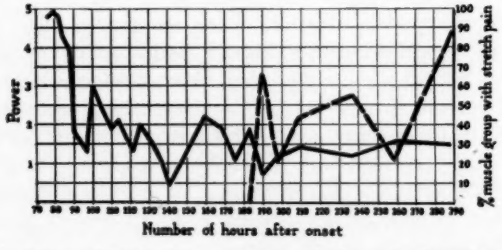

Fig. 2.—Evolution of paralysis and stretch pain for a single patient. The values for the average power of muscle groups is shown by the heavy line; the values for the percentage of muscle groups showing stretch pain, by the double broken line.

later, stretch pain and tenderness occurred only when about 80 per cent of the muscle groups were severely paralyzed. When, 109 to 114 hours after onset, both stretch pain and tenderness were noted in about 1 per cent of muscle groups examined, 70 per cent of the muscle groups were already severely paralyzed. The highest incidence of tenderness at any given time was 22 per cent, and that of stretch pain, 15 per cent. The late occurrence of stretch pain is illustrated

in figure 2, in which the evolution of paralysis and stretch pain in a single case is presented graphically. Despite the fact that 65 hours after admission and 56 hours after the first weakness was noted the average power of all the muscle groups was 0.5, stretch pain did not occur until 42 hours later. This figure will show that stretch pain does not precede paralysis but, rather, occurs when muscular power is improving.

Of 14 cases in which severe paralysis did not occur and in which the muscles usually remained unimpaired, tenderness was present at one time or another in 9 and stretch pain in 3, and in 5 cases, neither occurred. In 186 examinations of 32 muscle groups, or in a total of 5,952 evaluations, tenderness was noted in 94 instances, or in 1.5 per cent. In 2 cases, tenderness was noted 61 times; thus, in the remaining 12 cases and in 5,891 evaluations of muscle groups, tenderness was present in but 33 instances, or 0.55 per cent. Stretch pain occurred in 8 of 5,952 evaluations, a negligible number.

SUMMARY

A study was conducted consisting of successive examinations, day and night, of patients with acute anterior poliomyelitis from the time of their admission to the Municipal Contagious Hospital (Chicago) until discharge.

The results of this study showed that in no instance was there evidence of muscular spasm.

Tenderness occurred in 8 per cent of a group of 16 cases with resulting severe muscular paralysis, with a total of 2,919 muscle group examinations. At no time did it exceed 25 per cent.

In the same group stretch pain was elicited in only 3 per cent of 2,653 muscle group examinations. It never exceeded 15 per cent at any one time.

In a group of 14 cases in which the muscles remained unparalyzed or only slightly weak, tenderness occurred in only 1.5 per cent of 5,952 muscle group examinations, and stretch pain was practically absent.

Stretch pain and tenderness occurred more frequently in completely paralyzed muscle groups, but they were noted in only a small percentage of the total muscle group examinations during the development of paralysis.

Both tenderness and stretch pain occurred at a time when paralysis had fairly well progressed. With some exceptions, stretch pain usually began only when paralysis had reached its peak, and often when it had begun to recede.

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CONCLUSIONS

Muscular spasm is absent during the time of development of paralysis in acute anterior poliomyelitis.

Tenderness and stretch pain occur infrequently in muscle, and usually after paralysis has been well established.

Dr. Herman N. Bundesen, president of the Board of Health of the City of Chicago, and Dr. Archibald L. Hoyne, medical superintendent Municipal Contagious Disease Hospital, Chicago Board of Heaelth, permitted us to study the patients admitted to the hospital. Dr. Frederick Peters and Dr. John Wright, fellows in neurology of the Northwestern University Medical School, assisted in the study.

Northwestern University Medical School.

SO-CALLED AGENESIA OF THE CORPUS CALLOSUM (CALLOSAL DEFECT)

Anterior Cerebral Dysraphism

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THE MANY and varied concepts of defects, or agenesias, of the corpus callosum will be easily understood by a comparison of two recent papers on this subject. De Morsier and Mozer [1] suggested as an etiologic factor a disturbance during the closure of the anterior neuropore, as had previously been proposed by Marchand,[2] Goldstein [3] and Ernst.[4] De Morsier and Mozer [1] described a second type, in which an embryonal neoplastic agent, a lipoma or an angioma, destroys the corpus callosum (callosal body) during fetal life. Eventually, they claimed that disturbances in the vascularization of the lamina terminalis by the anterior callosal artery during fetal life was another cause. Kirschbaum,[5] on the contrary, suggested porencephaly as a cause of agenesia of the corpus callosum, whereby, in agreement with Yakovlev and Wadsworth,[6] an agenesia of the gyrus cinguli is the causative factor.

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† Dr. Marburg died June 13, 1948.

This paper was aided by a grant from the Dazian Foundation.

From the Department of Neurology, Columbia University College of Physicians and Surgeons.

1. de Morsier, G., and Mozer, J. J.: Agénésie complète de la commissure calleuse et troubles du développment de l'hémisphere gauche avec hémiparésie droite et intégrité mentale, Arch. Suisses de neurol. et psychiat. **35**:3, 1935.

2. Marchand, F.: Ueber die normale Entwicklung und den Mangel des Balkens in menschlichen Gehirn, Abhandl. d. math.-phys. kl. d. k. sächs. Gesellsch. d. Wissensch. **31**:371, 1909; Ueber den Mangel des Balkens im menschlichen Gehirn, Berl. klin. Wchnschr. **36**:182, 1899.

3. Goldstein, K.: Beiträge zur Entwickelungsgeschichte des menschlichen Gehirns, Anat. Anz. **22**:415, 1903; Zur Frage der Existenzberechtiguhg der sogenannten Bogenfasern des embryonalen menschlichen Gehirns nebst einigen weiteren Bemerkungen zur Entwicklung des Balkens und der Capsula interna, ibid. **24**:579, 1903.

4. Ernst, P.: Missbildungen des Nervensystems, in Schwalbe, E.: Die Morphologie der Missbildungen der Menschen und der Tiere, Vienna, G. Fischer, 1912, vol. 2, p. 141.

5. Kirschbaum, W. R.: Agenesis of the Corpus Callosum and Associated Malformations, J. Neuropath. & Exper. Neurol. **6**:78, 1947.

6. Yakovlev, P. I., and Wadsworth, R. C.: Schizencephalies, J Neuropath. & Exper. Neurol. **5**:116, 1946.

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In my paper presented at the annual meeting of the American Neurological Association in June 1947, I pointed out that all malformations in the region of the anterior neuropore, such as cyclopia, arhinencephaly and callosal defect, have a similar background, as was indicated also by Ernst,[4] and that they differ only in the period of fetal development which they represent. In addition, the damage must occur in the midline, as indicated by Marchand[2] and Goldstein,[3] though knowledge of the fetal development of this region was lacking at the time of their studies.

Before presenting my cases, I shall describe the development of the corpus callosum: Anterior to the lamina terminalis a slight thickening of the wall of the hemisphere appears in the midline—Hochstetter's[7] commissural plate. The raphe of the corpus callosum indicates a fusion of two plates in the midline, obviously occurring before the closure of the anterior neuropore. Evidence of this, however, is lacking. This plate is only a conduction tissue, called *Leitgewebe* by Held,[8] to facilitate the crossing of the fibers. These fibers are condensed dorsally as the corpus callosum and ventrally as the anterior commissure, whereas the remnant of the commissural plate between is represented by the septum pellucidum. Hochstetter[7] (fig. 1 *A*), however, overlooked the fact that the third interhemispheral commissure (Ammon's commissure), the psalterium, connecting the two hippocampal regions, also crosses within the commissural plate, being the main commissure in lower animals, whereas in higher animals the neopallial commissure, the corpus callosum, predominates. Streeter[9] stressed this difference between the archipallial and the neopallial commissures, and Tilney[10] showed the close relation of the psalterium to the corpus callosum, the former shifting caudally by the interpolation of callosal fibers from the frontal and parietal portions of the brain. Thus the corpus callosum, the anterior commissure and the psalterium, as well as the septum pellucidum, are integral parts of the commissural plate, a lesion of which, in the midline, will affect all these structures.

During the presence of the commissural plate—the first fourteen days of fetal life—the vascularization has not progressed far enough to enable one to speak of an anterior cerebral artery. From the capillary

7. Hochstetter, F.: Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns, Leipzig, F. Deuticke, 1919.

8. Held, H.: Zur Histogenese der Nervenleitung, Zentralbl. f. norm. Anat. u. Mikrotechn. **3**:165, 1906.

9. Streeter, G. L.: The Development of the Nervous System, in Keibel, I. K. J., and Mall, F. P.: Manual of Human Embryology, vol. 3, Philadelphia, J. B. Lippincott Company, 1912.

10. Tilney, F.: The Hippocampus and Its Relations to the Corpus Callosum. J. Nerv. & Ment. Dis. **89**:433. 1939.

network surrounding the origin of the neuraxis two branches of an artery appear; the posterior one fuses with vertebral branches to the basilar artery and is the main artery of early fetal life, and the anterior branch represents the anterior, as well as the middle, cerebral artery. Later, when the corpus callosum is fully developed, its rostrum and the ventrointernal portion of the genu, as well as the septum pellucidum and the internal portion of the column of the fornix, are supplied by the anterior communicating artery. The anterior cerebral artery supplies the region in front of the anterior commissure, as well as three fourths to four fifths of the corpus callosum, and the medial wall of the hemisphere to the precuneus and dorsally almost to the edge of the mantle. The posterior cerebral artery supplies the splenium and the adjacent portion of the corpus callosum (Goldstein[11]). As shown by this short survey, a vascular lesion must be restricted to certain circumscribed areas, but not to the septum pellucidum in particular.

REPORT OF CASES

Two brains showing this callosal defect are described.

CASE 1.—*Adult brain; no history available; all structures of the commissural plate absent.*

The section in figure 1 *B* corresponds to figure 64 of my atlas[12] (Reiley, fig. 316). The corona radiata at the left side ends like a plug, both dorsally and ventrally. The tapetum is present. All the convolutions, particularly the gyrus rectus and the dorsal and ventral cingular gyri, are present. The right ventral gyrus cinguli is somewhat atrophic. Although this region corresponds to the rostral portion of the callosal body, none of its fibers are present, but the convolutions are uninterrupted medially.

A section in the region of the columns of the fornix (fig. 1 *C*), shows a median split, with no trace of callosal fibers in the midline, as well as absence of fibers in the anterior commissure. The pillars of the fornix diverge dorsally and bend laterally above the caudate nucleus. There they meet a bundle of transversely cut fibers, which continue into a callosal rudiment. The transversely cut bundle of the anterior commissure is present ventrally within the putamen (left). The medial wall of the hemisphere is rolled inward, and the gyrus cinguli is present, though atrophic, in its most ventral portion.

Somewhat caudal to this section, two transveresly cut bundles above the caudate nucleus appear laterally in connection with a callosal rudiment (fig. 1 *D*). The inward rolling of the medial hemispheral wall is more pronounced, as is the atrophy of the gyrus cinguli. The indusium griseum is not clearly visible.

In the region of the medial commissure (fig. 2 *A*) only two transversely cut bundles above the caudate body are present. The lateral bundle on the left is larger

11. Goldstein, M.: Beitrag zur Anatomie und functionellen Bedeutung der Arterien des Gehirns insbesondere des Balkens, Ztschr. f. d. ges. Neurol. u. Psychiat. **26**:361, 1914.

12. Marburg, O.: Mikroscopischtopographischer Atlas der menschlichen Zentralnervenssystem, mit begleitendem Texte, ed. 2, Leipzig. F. Deuticke, 1910.

than the one on the right, where a small amount of gray matter lies at its base (stria longitudinalis lateralis). The atrophy of the gyrus cinguli is progressive. There is also pronounced dilatation of the pars centralis (cella media).

Shortly before the transition of the pars centralis into the posterior horn of the lateral ventricle (fig. 2*B*), the medial transversely cut bundle bends laterally and enters the fimbria, without any trace of the psalterium. The connections of both bundles are preserved, and the medial bundle is covered at the right side with

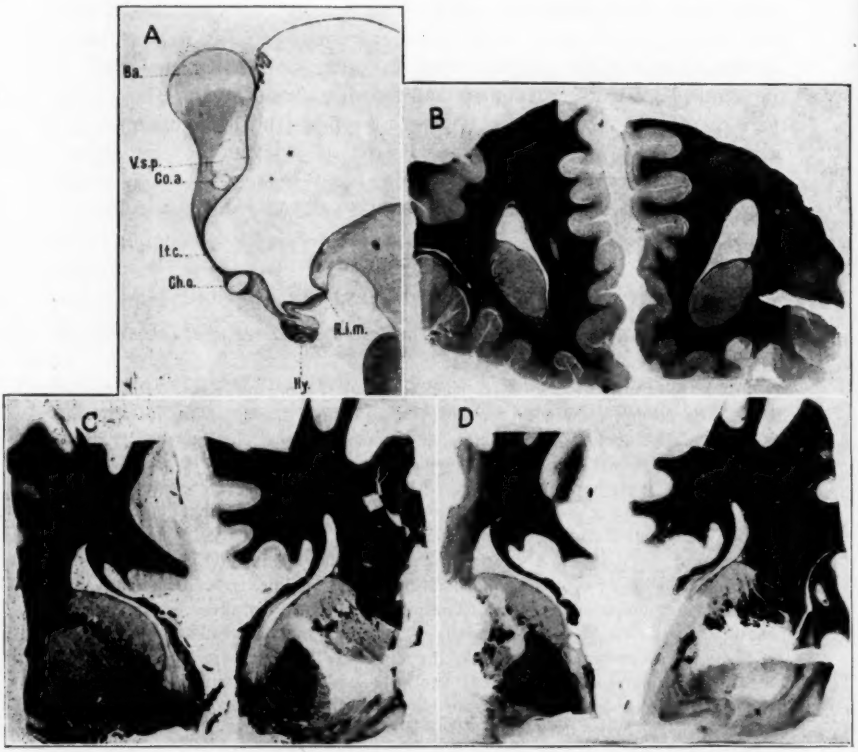

Fig. 1.—*A* (from Hochstetter [7]), sagittal section of a 100 mm. (crown-rump length) fetus. *Ba* indicates the corpus callosum; *Ch.o.* the optic chiasm; *Co.a.*, the anterior commissure; *Hy*, the hypophysis; *l.t.c.*, the lamina terminalis; *R.i.m.*, the recessus inframamillaris; *V.s.p.*, the ventriculus septi pellucidi.

B-D (case 1): *B*, region of the genu of the corpus callosum (the callosal fibers are indicated by dorsal and ventral plugs); *C*, region of the columns of the fornix (they are attached to callosal fibers laterally); *D*, two transversely cut bundles above the caudate nucleus, representing, laterally, the corpus callosum and, medially, the fornix.

angiomatous tissue, consisting of many wide, thick-walled, partially blood-filled vessels with connective tissue between, a structure normally not seen in this region.

Caudal to the latter section the transition of the lateral transversely cut bundle into longitudinal by coursing fibers is seen, and these fibers cover the central portion of the ventricle (fig. 2 *C*). The lateral wall of the ventricle shows the typical structure (tapetum). Medially, however, the large bundle fuses with the white matter of some small convolutions, which are difficult to identify. They give the impression of microgyria, but several small gyri are normally

Fig. 2.—*A*, longitudinal callosal bundle attached to the fornix. The bundle on the left is much larger than that on the right, where there is a small amount of gray matter at the base. *B*, bundle of the fornix shifting ventrally to form the fimbria. No psalterium is visible. *C*, longitudinal callosal bundle shifting ventrally to form the tapetum.

present (Retzius'[1] gyrus, gyrus fasciolaris). The gyri present in this case were characterized by a thick tangential layer, and in one of them there was a band corresponding to the fourth layer. But the sulci had a radial arrangement, and the architecture of the deep gray and white matter was almost normal.

CASE 2.—*Excessive hydrocephalus with tissue-thin hemispheral walls, somewhat thicker at their junction with the brain stem.*

The callosal rudiment appears normal but is shifted laterally as a result of dilatation of the third ventricle, as well as being stretched, owing to the pressure of fluid (fig. 3 *A*). Macroscopically, there were to be seen a bridge between the two hemispheres and the rudiment of a callosal body. In the region of the caudate nucleus and the putamen, separated by a well defined internal capsule, the medial

Fig. 3. (case 2).—*A*, a callosal rest in the midline; *B* (detail of *A*), the ventriculus septi pellucidi, the gap within the callosal rest.

bridge is covered dorsally by two convolutions, separated in the midline by a small split (gyrus cinguli). Ventrally, the convolutions are not recognizable, but the many foldings indicate a ventral gyrus cinguli, as well as a gyrus rectus (fig. 3 *B*). The bridge consists of glia with decussating myelinated fibers. A slight gap in its center obviously is the ventriculus septi pellucidi. Caudally this callosal rudiment was absent, but the crura fornicis, as well as a psalterium, was present.

There was in this case of extreme congenital hydrocephalus at least a rudiment of the corpus callosum. In cases of hydrocephalus of lesser degree the corpus callosum is present throughout, however thinned, but easily recognizable in all its portions.

Comment.—The first case represents a complete callosal defect in which a lesion in the fetal period destroyed all the structures of the commissural plate or impeded their decussation. Thus, there was no callosal body or crossing anterior commissure, no psalterium and no septum pellucidum. Since, according to Stockard,[13] the causes of malformations are almost irrelevant, high carbon dioxide and low oxygen concentrations being sufficient to serve as causative factors, it is apparent that only the period of developmental arrest, the time of development of the malformation, is important; since the commissural plate forms within the first fourteen days after conception, the period of development of the callosal defect in this case must have been at this time. All the other signs are sequelae. One could trace the transition of callosal fibers into the longitudinal callosal bundle, which increased in size toward the middle of the optic thalamus and decreased caudally. The fibers ended homolaterally at the medial, as well as the lateral, wall of the posterior and inferior horns of the lateral ventricle, and also, obviously, at the wall of the pars centralis. The end of the anterior commissure was not so easy to discern, since the commissure was very small. The fornix, which was in constant connection with the longitudinal callosal bundle, so that an exchange of fibers was probable, continued into the fimbria without a vestige of a hippocampal commissure. The inward rolling of the medial wall of the hemisphere was remarkable, and was obviously due to atrophy of the cingular gyrus in its middle portion, whereas the anterior and posterior portions of this gyrus appeared normal. The accompanying hydrocephalus was not great enough to explain the destruction of the callosal plate. The question whether there were microgyric changes in the region of the gyrus fasciolaris and the gyrus Retzii could not be decided.

In the second case, one can state only that, in spite of the extreme hydrocephalus, a callosal rudiment was present, as well as the psalterium, evidence that even extreme hydrocephalus cannot destroy the callosal body as a whole. The present remnants appeared not as arrest of development but, rather, as the result of a destructive process whereby those portions were preserved which were not so intensively exposed to pressure as the destroyed portions.

13. Stockard, C. R.: The Artificial Production of a Single Median, Cyclopean Eye in the Fish Embryo by Means of Sea Water Solution of Magnesium Chloride, Arch. f. Entwcklngsmechn. d. Organ. **24**:249, 1907.

GENERAL COMMENT

Ever since Anton [14] and, somewhat later, Marchand,[2] first described accurately the signs of callosal defect, all authors have been in agreement that, with the corpus callosum, the anterior commissure, the psalterium and the septum pellucidum are absent and that the gyrus cinguli is atrophic or absent, with the resulting inward rolling of the wall of the hemisphere and the radial arrangement of the sulci. The absence of the common section of the calcarine and the parieto-occipital fissure is also stressed. The hydrocephalus, which, according to Virchow [15] and Anton,[14] is the cause of this process, is present in most cases and is best seen in the posterior horn, leading to the erroneous explanation that the absence of the splenial fibers is a causative factor. The only additional structure described was an occipitofrontal longitudinal bundle, first noted by Forel-Onufwrowicz,[16] and recognized by Probst,[17] as consisting of aberrant callosal fibers—heterotopic fibers, as LaSalle-Archambault [18] called them, the longitudinal callosal bundle (*Balkenlängsbündel*).

It is obvious that not all cases of callosal defect correspond to mine, which represented a typical, as well as a complete, defect. In many of the cases there was cyclopia or arhinencephaly. Mingazzini [19] found only 43 cases of complete callosal defect in a series of 71 cases. Since his review, many cases have been published (Trétiakoff and Balestra [20]; de Lange [21]; Bertrand and Hatzigeorgiou [22]; von Hayek [23];

14. Anton, G.: (*a*) Zur Anatomie des Balkenmangels im Grosshirn, Ztschr. f. d. allg. Heilk. **7**:53, 1886; (*b*) Die Bedeutung des Balkenmangels für das Grosshirn, Klin. Wchnschr. **9**:1031, 1896.

15. Virchow, R.: Ueber ein Gehirn mit Balkenmangel, Neurol. Centralbl. **6**:263, 1887.

16. Forel-Onufwrowicz, W.: Das balkenlose Mikrocephalengehirn Hofmann, Arch. f. Psychiat. **18**:305, 1887.

17. Probst, M.: Ueber den Bau des balkenlosen Grosshirns, sowie über Mikrogyrie und Heterotopie der grauen Substanz, Arch. f. Psychiat. **34**:709, 1901.

18. LaSalle-Archambault: Contribution à l'anatomie et la pathogénie de la soidisant agénésie du corps calleux, Nouv. iconog. de la Salpêtrière **23**:630, 1910.

19. Mingazzini, G.: Sopra un encefalo con arresta di sviluppo, appartenente ad un idiota di eleven mesi, Internat. Monatschr. f. Anat. u. Physiol. **7**:171, 1896; Der Balken, Berlin, Julius Springer, 1922.

20. Trétiakoff, C., and Balestra, S.: Absence congénitale du corps calleux sans troubles psychique apparents chez une femme morte à l'âge de 32 ans, Bull. Soc. clin. de méd. ment. **10**:58, 1922.

21. de Lange, C.: On Brains with Total and Partial Lack of the Corpus Callosum and of the Nature of the Longitudinal Callosal Bundle, J. Nerv. & Ment. Dis. **62**:449, 1925.

Gutmann [24]; Stringaris [25]; Thomas [26]; Huddleson [27]; Rubinstein [28]; Hinrichs [29]; Baker and Graves [30]; Segal [31]; Josephy [32]; Foerster [33]; de Morsier and Mozer [1]; Lloyd and Jacobsen [34]; Reeves and Courville [35]; Shryock, Bernard and Knighton [36], and, eventually, Kirschbaum [5]). With the cases discovered roentgenologically, almost 100 have now been accurately studied. Like the cases collected by Mingazzini, however, they are not all of the same kind. In many instances the anterior commissure is present but all of the other signs are manifest, as in cases of complete callosal defect (Hagen,[37] Malinverni,[38]

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22. Bertrand, J., and Hatzigeorgiou, G.: Etude anatomique d'un cas d'agénésie du corps calleux, Rev. neurol. **51**:77, 1929.

23. von Hayek, H.: Ueber einen Fall von Hypoplasie des Balkens an einem in situ gehärteten Gehirn eines Neugeborenen, Virchows Arch. f. path. Anat. **273**: 767, 1929.

24. Gutmann, L.: Ueber einen Fall von Entwicklungshemmung des Gross- und Kleinhirns mit Balkenmangel, Psychiat.-Neurol. Wchnschr. **31**:453, 1929.

25. Stringaris, M. G.: Mikrencephalie, Frankfurt. Ztschr. f. Path. **37**:396, 1929.

26. Thomas, A.: A propos d'un cas d'absence congénitale du corps calleux sur le cerveau humain, Arch. d'anat., d'histol. et d'embryol. **10**:347, 1929.

27. Huddleson, G. H.: Ein Fall von Balkenmangel mit Lipomentwicklung im Defect, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:177, 1928.

28. Rubinstein, B. G.: Ueber eine Fall von unvollständig fehlendem und durch Fettgewebe ersetzten Balken, Frankfurt. Ztschr. f. Path. **44**:379, 1932.

29. Hinrichs, U.: Ueber eine durch Balken und Fornixmangel ausgezeichnete Gehirnmissbildung, Arch. f. Psychiat. **89**:57, 1929.

30. Baker, R. C., and Graves, G. O.: Partial Agenesis of the Corpus Callosum, Arch. Neurol. & Psychiat. **29**:1054 (May) 1933.

31. Segal, M.: Agenesia of the Corpus Callosum in Man, South African J. M. Sc. **1**:65, 1935.

32. Josephy, H.: Congenital Agyria and Defect of the Corpus Callosum, J. Neuropath. & Exper. Neurol. **3**:63, 1944.

33. Foerster, O.: Ein Fall von Agenesie des Corpus callosum verbunden mit einem Diverticulum paraphysarium des Ventriculus tertius, Ztschr. f. d. ges. Neurol. u. Psychiat. **164**:380, 1939.

34. Lloyd, J. S., and Jacobsen, J. N.: Agenesis of the Corpus Callosum, J. Ment. Sc. **84**:995, 1938.

35. Reeves, D. L., and Courville, C. B.: Complete Agenesis of the Corpus Callosum, Bull. Los Angeles Neurod. Soc. **3**:169, 1938.

36. (*a*) Shryock, H., and Knighton, R. S.: Arhinencephaly with Associated Agenesis of the Corpus Callosum and Other Anomalies, Bull. Los Angeles Neurol. Soc. **5**:192, 1940. (*b*) Shryock, H.; Bernard, J. F., and Knighton, R. S.: Agenesis of the Corpus Callosum, ibid. **5**:146, 1940.

37. Hagen, R.: Zwei Fälle von Idiotie, Allg. Ztschr. f. Psychiat. **29**:688, 1873.

38. Malinverni: Cervello d'uomo mancanto di corpo calloso, Torino, 1874; cited by Mingazzini.[19]

Knox,[39] Eichler,[40] Forel-Onufwrowicz [16] Kaufmann,[41] Deny,[42] Bruce,[43] Probst,[17] Cameron,[44] LaSalle-Archambault,[18] Klieneberger [45] and Stoecker,[46] Kino,[47] Hulkrantz,[48] Meyer,[49] de Lange,[21] Lloyd and Jacobsen,[34] Reeves and Courville [35] and Kirschbaum [5]). Eichler [40] described a small plate at the side of the corpus callosum, and in Probst's,[17] as well as in Gutmann's,[24] case the callosal fibers approached the midline, without crossing it. In some of the cases the anterior commissure was larger than normal, as described in cases of arhinencephaly by de Jong.[50] This author suggested that some callosal fibers detour via the anterior commissure (Paget, [51] Huppert,[52] Malinverni,[38] Trétiakoff and Balestra,[20] Bertrand and Hatzigeorgiou [22] and Reeves and Courville [35]). Occasionally, some portions of the septum pellucidum are also preserved (Eichler [40]; Forel-Onufwrowicz [16]). The absence of the psalterium was first described by Poterin-Dumontel,[53] and later by LaSalle-Archambault,[18] Kino [47] and many others.

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39. Knox, D. N.: Description of a Case of Defective Corpus Callosum, Glasgow M. J. **10**:227, 1875; cited by Bruce.[43]

40. Eichler, G.: Ein Fall von Balkenmangel in menschlichen Gehirn, Arch. f. Psychiat. **8**:355, 1878.

41. Kaufmann, E.: Ueber Mangel des Balkens im menschlichen Gehirn, Arch. f. Psychiat. **18**:769, 1887; **19**:229, 1888.

42. Deny: Note sur un cas d'imbecillité, Nouv. iconog. de la Salpêtrière, **1**:100, 1888.

43. Bruce, A.: On the Absence of the Corpus Callosum in the Human Brain with the Description of a New Case, Brain **12**:171, 1889.

44. (*a*) Cameron, J. A., and Nicholls, A. J.: Two Rare Abnormalities Occurring in the Same Subject: Partial Absence of the Corpus Callosum and the Stomach Situated Entirely Within the Thorax, Canad. M. A. J. **11**:408, 1921. (*b*) Cameron, J.: A Brain with Complete Absence of the Corpus Callosum, J. Anat. & Physiol. **41**:293, 1906.

45. Klieneberger, O. L.: Ein Fall von Balkenmangel bei juveniler Paralyse, Allg. Ztschr. f. Psychiat. **67**:572, 1910.

46. Stoecker, W.: Ueber Balkenmangel im menschlichen Gehirn, Arch. f. Psychiat. **50**:543, 1913.

47. Kino, F.: Ueber Balkenmangel, Ztschr. f. d. ges. Neurol. u. Psychiat. **62**:163, 1920.

48. Hulkrantz, J. V.: Ueber die Hirnfunctionen bei Agenesie des Balkens, Upsala läkaref. förh. **26**:1, 1921.

49. Meyer, O.: Kompletter Balkenmangel, Centralbl. f. allg. Path. u. path. Anat. **35**:267, 1924.

50. de Jong, H.: Ueber Arhinencephalie mit Hypertrophieen im Gehirn, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:734, 1927.

51. Paget, J.: Account of a Case in Which the Corpus Callosum, Septum Lucidum and Fornix Were Incompletely Formed, Lancet **1**:337, 1846; Med.-Chir. Tr. **29**:55, 1846.

52. Huppert, M.: Ein Fall von Balkenmangel bei einem epileptischen Idioten, Arch. f. d. allg. Heilk. **12**:243, 1871.

53. Poterin-Dumontel: Absence congénitale du corps calleux sans troubles fonctionnels durant la vie, Gaz. d. hôp. **36**:47, 1863.

Only in Kaufmann's case [41] were the two hemispheres fused. In some cases the absence of the gyrus cinguli was without doubt, but usually only atrophy was noted, as in my first case. Although Malinverni,[38] Knox,[39] Kaufmann,[41] Probst [17] and LaSalle-Archambault [18] mentioned complete absence of the gyrus cinguli, interruption in the middle part of this gyrus was noted by de Lange,[21] whereas Stoecker [46] stated that in Klieneberger's [45] case there was a distinct gyrus fornicatus, and Kino,[47] made a similar claim in his case at least on the left side. The radial arrangement of the sulci may also be absent (Cameron and Nicholls [44a]).

In the present case the fibers of the longitudinal bundle of the corpus callosum also ended in the pars centralis, as well as forming an intimate connection with the fornix, which may be an exchange of fibers, as stated by Probst.[17]

In a third group of cases, a small anterior bridge, a callosal rudiment, is present (Down,[54] Landsberger,[55] Eichler [40]); its fibers may be myelinated in some cases (Marchand,[2] Arndt and Sklarek,[56] Mingazzini [19]). It may also be that the case of de Morsier and Mozer [1] belongs in this group, though the authors compare a small interseptal commissure with the commissura pallii of lower animals, which, however, is a commissure of the fornix—a ventral psalterium.

In some cases somewhat more of the callosal body is preserved (Jolly,[57] Anton,[14b] Grosz,[58] de Lange,[21] Rubinstein [28]); the rostrum and genu and the rest of the absent portion are replaced by a longitudinal callosal bundle. In the case of Cameron and Nicholls,[44a] the corpus callosum ended ½ inch (1.25 cm.) caudal to the genu, but in all the cases mentioned the characteristic signs of total callosal defect were present.

The latter fact is evidence that these cases differ only in the completeness of the defect, and that the agenesis should be traced back to a fetal lesion of the commissural plate. This explanation does not hold

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54. Down, J. L. H.: Case in Which the Corpus Callosum and the Fornix Were Imperfectly Formed and the Septum Lucidum and Commissura Mollis Were Absent, Proc. Roy. M. & Chir. Soc. **3**:404, 1861; cited by Bruce.[43]

55. Landsberger, F.: Ueber Balkenmangel, Ztschr. f. d. ges. Neurol. u. Psychiat. **11**:515, 1912.

56. Arndt, M., and Sklarek, F.: Ueber Balkenmangel in menschlichen Gehirn, Arch. f. Psychiat. **38**:756, 1903.

57. Jolly, F.: Ein Fall von mangelhafter Entwicklung des Balkens im menschlichen Gehirn, Ztschr. f. rat. Med. **36**:4, 1869.

58. Grosz, D.: Mikrogyrie und Balkenmangel im menschlichen Gehirn, Arch. f. Psychiat. **45**:605, 1909.

true for the cases of Mitchell,[59] Foerg,[60] Zingerle[61] and Shryock, Bernard and Knighton,[36] and for 1 of Kirschbaum's[5] cases. In the cases of Mitchell,[59] Foerg[60] and Zingerle[61] the longitudinal callosal bundle was absent, and the authors mention as an etiologic factor an injury in early childhood or during the fetal period. In the case of Shryock, Bernard and Knighton,[36b] porencephaly around the sylvian fissure on both sides destroyed the corpus callosum and the septum pellucidum, as well as the hippocampal commissure. The absence of a longitudinal callosal bundle places this case with those of secondary destruction of the structures mentioned, followed by secondary degeneration of all the affected structures, a process representing a much later period of arrested development. Kirschbaum's[5] second case is obviously of the same type (porencephaly in the occipital lobe, internal microgyria [heterotopia] of the frontal lobes.) The 3 cases of Sander,[62] with atrophy of the splenium, are also instances of secondary destruction, since extreme microgyria of the occipital lobe was present in his first case and micrencephaly in the others.

Quite different from these cases of secondary destruction of the corpus callosum are cases in which this commissure is connected with all portions of the cortex but is restricted in length as well as in width, a condition comparable to the development of this structure in the fourth month of fetal life. Paget[51] first described such a case of arrested development; Marchand,[2] Rubinowitsch and Barbé[63] and von Hayek[23] later described similar cases.

It is impossible to agree with de Morsier and Mozer[1] in their assumption that a fetal neoplasm in the region of the lamina terminalis causes destruction of the corpus callosum. One cannot study cases of such tumors without referring to cases of similar neoplasms in the region of the posterior neuropore, during the closure of which mesenchyme slips into the neural tube, resulting in the formation of lipoma, fibroma or angioma, according to the nature of the displaced cells. A similar

59. Mitchell, H.: Description of the Dissection of a Brain in Which the Corpus Callosum, Fornix, and Septum Were Imperfectly Developed, Med.-Chir. Tr. **31**:239, 1848.

60. Foerg: Die Bedeutung des Balkens im menschlichen Gehirn, Munich, J. Deschler, 1855; cited by Bruce.[48]

61. Zingerle, H.: Ueber die Bedeutung des Balkenmangels im menschlichen Grosshirn, Arch. f. Psychiat. **30**:400, 1896.

62. Sander, J.: Ueber Balkenmangel im menschlichen Gehirn, Arch. f. Psychiat. **1**:128, 1868.

63. Rubinowitsch. J., and Barbé, A.: Un cas d'agénésie du corps calleux, Nouv. iconog. de la Salpêtrière **26**:407, 1913.

situation is that of the anteror neuropore, since in this region there are also displaced germinal cells, in Cohnheim's sense. My former pupil Krainer [64] collected 22 cases of lipoma in this region, but missed the one reported by Jolly [57] and Rubinstein.[28] Kirschbaum [5] observed a meningioma, and Creutzfeld and Simons,[65] as well as Stewart and Ross,[66] observed angiomas. The most important point in these cases, however, is the fact that in spite of the tumor the defective structures, as well as the sequelae, are identical with those associated with complete absence of the corpus callosum. Particularly, the arrangement of the sulci of the medial wall of the hemispheres is similar to that in cases of callosal defect. The tumor does not destroy the corpus callosum; it only complicates a developmental disturbance.

A small angioma was seen in my first case; caudally, it lay almost within the meninges. The case of Stewart and Ross [66] is questionable, since the signs of tumor developed after trauma. There were a varix and an aneurysm, and the characteristic signs of a callosal defect (absence of convolutions and longitudinal bundle) were not present.

With regard to vascular lesions as a cause of callosal defect, as suggested by Sander,[62] Bruce,[48] and, particularly, de Morsier and Mozer,[1] such a lesion may destroy the corpus callosum, in part at least, as evidenced by hemorrhages or malacias in the structure (Mingazzini [19]). But such a process is circumscribed, and in the traumatic cases mentioned (Mitchell,[59] Zingerle,[61] Foerg [60]) the agenesis may have been of vascular origin.

But, as noted at the beginning of this paper, the vascularization of the corpus callosum in fetal life is variable and the anterior cerebral artery forms only part of it. It is not true, as de Morsier and Mozer [1] stated, that a callosal defect is due to a lesion of this artery. On the contrary, initally the anterior and middle cerebral arteries are represented by one branch, so that a lesion of this vessel must be followed by simultaneous disturbance in the medial, as well as the lateral, hemispheral wall, a condition which has not been noted in any of the known cases of complete callosal defect. Moreover, an inflammatory process is not sufficiently circumscribed to destroy the extremely small region of the commissural plate.

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64. Krainer, L.: Die Hirn- und Rückenmarkslipome, Virchows Arch. f. path. Anat. **295**:107, 1935.

65. Creutzfeld, and Simons: Zur Frage der Balkenbildung, Zentralbl. f. d. ges. Neurol. u. Psychiat. **57**:854, 1930.

66. Stewart, R. A., and Ross, A. W.: Angioma Arteriale Racemosum in an Acallosal Brain, J. Neurol. & Psychopath. **11**:289, 1930.

In some cases the vascular lesion is a complicating factor, or the callosal defect is the sequela of a vascular lesion. To this group belong all cases of cyst formation and porencephaly, even microgyria and heterotopias. Such cases are characterized by a localized process in the middle cerebral artery with unilaterial hydrocephalus and contralateral hemiplegia (Landsberger,[55] Kino [47]). In Probst's [17] case the process also affected portions of the anterior cerebral artery, as it did in the case of Shryock, Bernard and Knighton.[36b] The cyst formation in Grosz's [58] case was due, according to the author, to an encephalitic process.

In such cases of vascular disturbance it is difficult to decide whether there is true microgyria, pseudomicrogyria or any microgyria at all. The same is true of heterotopias, since, for example, in the cases reported by LaSalle-Archambault [18] or de Morsier and Mozer,[1] the heteropia was obviously an internal microgyria. The case of the latter authors was not exceptional. Since there was a localized process in the left frontal lobe, the hemispheral atrophy was due to the arrest of development seen in every case of a fetal lesion. It is interesting that in most of the cases cited the callosal arteries were intact. In the case of de Morsier and Mozer,[1] however, the right anterior cerebral artery was present and the left was absent, but in their figure 10 many branches of this artery supplied the medial hemispheral wall, as well as the corpus callosum.

In our paper on porencephaly,[67] my associates and I proved false the concept of Yakovlev and Wadsworth [6] of a secondary encephaloclastic type and a type representing a true developmental failure—an agenesis of the convolutions. Kirschbaum [5] referred to this theory when he stated:

> The cleft resulting from the failure of the corpus callosum to develop and the appearance of the medial convolutions is comparable with the radial, or stellate and parallel, convolutions around certain early porencephalic lesions of the hemispheres.

On these remote similarities, Kirschbaum based the following by hypothesis: Agenesia of the corpus callosum is a schizencephaly (early porencephaly), a disturbance confined to the midsagittal line. All authors agree that porencephaly is not a lesion of early development and that the callosal anlage appears early in fetal life. Development of porencephaly coincides with the second half of fetal life; that of the callosal anlage, with a very early stage in the first half, that of the closure of the neuropore.

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67. Marburg, O.; Rezek, P. R., and Marks, M. B.: Porencephaly, J. Neuropath. & Exper. Neurol. **4**:43, 1945.

What is true for porencephaly is true also for hydrocephalus, a condition which is not, as Virchow [15] and Anton [14] suggested, a causative factor, but a supporting one. As proof of this statement is the occurrence of cases with relatively slight, or even no, hydrocephalus (Hochhaus [68]). Also evidence is my second case, in which a callosal rudiment was observed in the region where the pressure of the fluid was the least.

Of all the signs observed in cases of callosal defect, the absence or atrophy of the cingular gyrus has caused the most difficulty. Except for the fact that the hemispheres in typical cases may be entirely normal (Forel-Onufwrowicz [16]), Marchand's [2] description is correct. The atrophy or absence of the gyrus cinguli causes an inward rolling of the hemisphere; the sylvian fissure is widened, and the edge of the mantle is shifted medially and ventrally, accounting for the radial arrangement of the sulci. There is an analogous process in arhinencephaly, in which, with the absence of the olfactory bulb and tract and of the stria olfactoria, the gyrus rectus also is destroyed or becomes atrophic. The convolutions near the focus, and closely connected with it, are subject to the same fate.

SUMMARY

It is shown that all cases of callosal defect are not of the same origin. One type is due to a developmental disturbance of the commissural plate. This type is characterized by the absence or, in cases of less intensity and extent, by partial absence or reduction of the structures in the midline: the corpus callosum, the anterior commissure, the psalterium and the septum pellucidum. In all the cases the callosal fibers are heterotopic and appear as a longitudinal bundle. The gyrus cinguli in its middle position is either absent or atrophic, resulting in the radial arrangement of the sulci of the medial wall of the hemisphere, as well as the absence of the common section of the parieto-occipital and the calcarine fissure. Eventually, hydrocephalus develops. This true callosal defect may be called telencephaloschisis, according to de Morsier and Mozer [1]; and, because cyclopia and arhinencephaly belong to the same group, telencephaloschisis restricta. Since, however, the process close to the anterior neuropore is similar to that at the posterior neuropore, one might speak of araphism or dysraphism anterior in accordance

68. Hochhaus, H.: Ueber Balkenmangel im menschlichen Gehirn, Deutsche Ztschr. f. Nervenh. **4**:79, 1893.

with the term used by Henneberg and Koch [69] for the defect involving the posterior neuropore.

All cases in which the defect is due to arrested development, vascular lesions, inflammation, hydrocephalus or porencephaly differ from the cases of genuine callosal defect, and the malformation is secondary, even if it occurs in fetal life. The defect develops in the second half of fetal life, whereas the genuine type develops within the first fourteen days after conception.

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69. Henneberg, R., and Koch, M.: Zur Pathogenese der Syringomyelie und über Hämatomyelie bei Syringomyelie, Monatschr. f. Psychiat. u. Neurol. **54**:117, 1923.

News and Comment

THE AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology has been established to further and encourage the practice of clinical neurology and to stimulate teaching and research in neurology and allied sciences.

Active membership in the Academy is open to every physician who has been certified in neurology or in both neurology and psychiatry. Junior membership is available to physicians presently engaged in postgraduate studies in neurology or who are awaiting certification in neurology. In addition, there is an associate membership for those who are not certified in neurology but whose interests are in fields related to neurology. It is hoped that, because of the unrestricted membership, this association will be representative of the entire specialty of neurology and will offer an organ of expression for many of the younger men in the field. The American Academy of Neurology at present has 500 members. The first business meeting was held in Chicago in June 1948.

The first scientific meeting will be held at the French Lick Springs Hotel, French Lick Springs, Ind., on Wednesday, Thursday and Friday, June 1, 2 and 3, 1949. Dr. Dave B. Ruskin, of the Caro State Hospital, Caro, Mich., is in charge of the scientific program.

The present executive council consists of Dr. A. B. Baker, Minneapolis, president; Dr. Pearce Bailey, Washington, D. C., vice president; Dr. Joe R. Brown, Minneapolis, secretary-treasurer, and Dr. Frederick Lewey, Philadelphia; Dr. William A. Smith, Atlanta; Dr. J. M. Nielsen, Los Angeles, and Dr. A. L. Sahs, Iowa City, trustees. Communications to the Academy should be addressed to Dr. Joe R. Brown, 19 Millard Hall, University of Minnesota, Minneapolis 14.

INTERNATIONAL CONGRESS OF PSYCHIATRY

The International Congress of Psychiatry will be held in Paris, Oct. 4 to 12, 1950. In accordance with regulations decided on at the International preparatory meeting (Paris, Oct. 23, 1947), the official spoken languages will be English, French, Spanish and (should Russia participate) Russian.

The program of the six main afternoon sessions follows:

1. General Psychopathology. Session's chairman: Prof. Ferdinand Morel (Geneva, Switzerland): Subject: "Psychopathology of Delusions."

2. Clinical Psychiatry. Session's chairman: Prof. Honorio Delgado (Lima, Peru). Subject: "Application of Testing Methods to Clinical Psychiatry."

3. Psychiatric Anatomophysiology. Session's chairman: Prof. F. L. Golla (Bristol, England). Subject: "Cerebral Anatomy and Physiology in the Light of Lobotomy and Topectomies."

4. Psychiatric Biologic Therapy. Session's chairman: Prof. Jozef Handelsman (Warsaw, Poland). Subject: "Respective Indications for the Shock Therapy Methods."

5. Psychotherapy; Psychoanalysis; Psychosomatic Medicine. Session's chairman: Dr. Franz Alexander (Chicago, United States). Subject: "Evolution and Present Trends of Psychoanalysis."

6. Social Psychiatry. Session's chairman: Prof. Torsten Sjögren (Stockholm, Sweden). Subject: "Genetic and Eugenic Aspects of Psychiatry."

In addition, these six sections and the seventh section (Child Psychiatry) will organize for the morning sessions a number of meetings, symposiums and work sessions.

The organization committee plans to set up two exhibits in connection with the Congress—the first one on "art and psychopathology" (Dr. Bessière, Centre Psychiatrique Ste-Anne, I, rue Cabanis, Paris XIV°), and the second on "History of Psychiatric Progress" (Professor Laignel-Lavastine, .12bis, place Laborde, Paris VIII°).

The French committee was entrusted, at the International preparatory meeting, with the organization of the Congress. This committee, set up in 1947, is as follows: honorary chairmen, Prof. Pierre Janet (in memoriam), Prof. Jean Lhermitte (Paris); chairman, Prof. Jean Delay (Paris); vice chairmen, Dr. L. Marchand (Paris), Dr. Henri Baruk (Paris), Prof. P. Delmas-Marsalet (Bordeaux), Dr. Georges Heuyer (Paris); general secretary, Dr. Henri Ey (Paris); treasurer, Dr. P. Sivadon (Ville-Evrard, Neuilly-sur-Marne, Seine & Oise).

In each country, a national committee of the Congress is being set up; when possible, a chairman, a secretary and a director are appointed for each section.

Information may be obtained from General Management; Dr. Henri Ey, general secretary, I, rue Cabanis, Paris XIV°.

LESTER N. HOFHEIMER RESEARCH AWARD

In memory of the late Lieut. Lester N. Hofheimer, his estate has contributed a fund to the American Psychiatric Association for the purpose of providing an annual reward for an outstanding research accomplishment in the field of psychiatry and mental hygiene.

A group consisting of eight fellows of the Association, known as "The Hofheimer Prize Board," has been appointed to evaluate research papers and books submitted for consideration. This board is authorized to award each year, at the annual meeting of the American Psychiatric Association, a prize in the amount of $1,500, which will be known as "The Hofheimer Prize."

The conditions are as follows:

1. The award shall apply only to work published within a period of three years prior to the date of the award.

2. The granting of the award shall not be confined to fellows or members of the American Psychiatric Association, but shall be limited to citizens of the United States and Canada.

3. The recipient of the award must not be over 40 years of age at the time of his publication, or submission for publication, of a notable research in the field of psychiatry.

4. The award may be made to each member of a group instead of to an individual, provided that the majority of the group members are citizens of the United States or Canada and that the median age of the group does not exceed 40 years at the time of publication.

5. Ten copies of the published (article or book) should be in the hands of the board by March 1, 1949, that the recipient of the prize may be selected and the award presented at the next annual meeting of the Association. In subsequent years the material submitted for consideration should reach the Board no later than December 31.

All communications should be addressed to "The Hofheimer Prize Board," American Psychiatric Association, Office of Medical Director, 1624 Eye Street, N. W., Washington 6, D. C.

EXPANSION OF PSYCHIATRIC AND NEUROLOGIC TEACHING AND RESEARCH PROGRAMS AT THE NEW YORK UNIVERSITY-BELLEVUE MEDICAL CENTER

The New York University is expanding its postgraduate and graduate teaching facilities in psychiatry and neurology. Recently, the New York Post-Graduate Hospital was amalgamated with the New York University–Bellevue Medical Center. Simultaneously, the New York University announced the formation of a new Postgraduate School of Medicine, in addition to its already existing College of Medicine.

Dr. S. Bernard Wortis, in addition to his present position as professor of psychiatry and chairman of the department in the New York University College of Medicine, has been appointed professor of psychiatry and neurology in the Postgraduate School of Medicine and director of the psychiatric and neurologic services of the New York University Post-Graduate Hospital. He has, accordingly, relinquished administrative responsibility as director of the Bellevue Psychiatric Division and will be, after Jan. 1, 1949, consultant in psychiatry and neurology to the Bellevue Psychiatric Division. Dr. Lewis I. Sharp, who is associate professor of clinical psychiatry at the New York University, will assume the position of director of the Bellevue Psychiatric Division. This new arrangement will facilitate the coordination of the postgraduate and undergraduate training and research programs in psychiatry and neurology.

In addition, Dr. Morris Herman, associate professor of psychiatry, has relinquished his position as assistant director of the Bellevue Psychiatric Division in order to do full time psychiatric teaching and research in both the postgraduate and the undergraduate Colleges of Medicine. He will be visiting psychiatrist and neurologist to the Bellevue Psychiatric Division and will also be on the visiting staff of the University Post-Graduate Hospital.

These staff changes will permit an expansion of the New York University–Bellevue Medical Center's comprehensive program for training in psychiatry and neurology in the undergraduate and postgraduate Colleges of Medicine and their related clinical hospital services.

WING R, PSYCHIATRIC CLINIC, STRONG MEMORIAL HOSPITAL, THE UNIVERSITY OF ROCHESTER SCHOOL OF MEDICINE AND DENTISTRY

The dedication of Wing R, Psychiatric Clinic, of the Strong Memorial Hospital will be held Thursday, March 31, 1949, in the Upper Strong Auditorium, River Campus, the University of Rochester. The program is as follows:

MORNING SESSION: 10:30 A. M.

Presiding officer: Donald W. Gilbert, provost, University of Rochester

INTRODUCTORY REMARKS

George H. Whipple, dean, University of Rochester, School of Medicine and Dentistry

John Romano, professor of psychiatry, University of Rochester

BIOLOGIC BASIS OF ADAPTATION

Paul Weiss, professor of zoology, University of Chicago

ORGANISM AND ENVIRONMENT: DYNAMIC OPPOSITIONS

Homer W. Smith, professor of physiology, New York University

AFTERNOON SESSION: 2:30 P. M.

Presiding officer: John Romano, professor of psychiatry, University of Rochester

ADAPTATION ON THE THRESHOLD OF INTELLIGENCE

Howard Liddell, professor of psychobiology, Cornell University

THE NEUROTIC POTENTIAL AND HUMAN ADAPTATION
Lawrence S. Kubie, clinical professor of psychiatry and mental hygiene, Yale University; member of the faculty, New York Psychoanalytic Institute

ADJUSTMENT AND ADAPTATION: AN ANTHROPOLOGIC APPROACH
Clyde Kluckhohn, professor of anthropology, Harvard University

FIRST WESTERN INSTITUTE OF EPILEPSY

The First Western Institute on Epilepsy will meet in Denver at the University of Colorado Medical Center, May 16, 17 and 18, 1949. Members of the medical profession, as well as social workers, psychologists and interested laymen, are invited to attend. Lectures, clinics and round table discussions on epilepsy will be held, led off by Dr. Jerry Price, of the Neurological Institute, as keynote speaker. Institute fees will be $5. Requests for information may be addressed to the Director, Epilepsy Service, University of Colorado Medical Center, Denver.

FELLOWSHIP IN CHILD GUIDANCE CLINIC PSYCHIATRY

The American Association of Psychiatric Clinics for Children offers fellowships for training in child guidance clinic psychiatry. These fellowships are made possible financially by the United States Public Health Service and sometimes by local funds. In addition, a few communities are offering to finance the training of psychiatrists who will engage to work for them on a contractual basis for a given period following their training. The training is for positions in community clinics where psychiatrists, psychologists, social workers and others collaborate in the treatment of children suffering from emotional illnesses.

Most of the fellowships are for two years; some are for one. The stipend is in the neighborhood of $3,000 for the first year and about $3,600 for the second. The awarding of the fellowship for the second year is always dependent on the quality of the first year's work. Prerequisites are graduation from an approved medical school, a general internship and two years of approved general psychiatry (and personal qualifications essential for such work).

Opportunity is provided for the fellow to develop his own skills in a well organized outpatient service with the support of a carefully planned training program and adequate supervision. The training centers are selected on the basis of standards which have been established by the American Association of Psychiatric Clinics for Children, and the fellowships are awarded by a committee of this organization.

For further information, write to Dr. A. Z. Barhash, executive assistant, The American Association of Psychiatric Clinics for Children, 1790 Broadway (Room 916), New York 19.

POSTGRADUATE COURSE IN PSYCHIATRY AND NEUROLOGY, UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL

A postgraduate course of twelve weeks in psychiatry and neurology will be offered at the University of California Medical School (the Langley Porter Clinic), in San Francisco, Aug. 29 through Nov. 18, 1949, full time, under the chairmanship of Karl M. Bowman, M.D., professor of psychiatry, University of California. The fee will be $200. For program and information, kindly communicate with Stacy R. Mettier, M.D., head of postgraduate instruction, Medical Extension, University of California Medical Center, San Francisco 22.

Obituaries

ROSS McCLURE CHAPMAN, M.D.
1881-1948

After a devoted service to psychiatry of over forty-two years, Dr. Ross McClure Chapman died on Sept. 24, 1948, in the Union Memorial Hospital, Baltimore, of a protracted illness, at the age of 67. His wife, a sister and a half-sister survive him.

Dr. Chapman was born in Belleville, Jefferson County, N. Y., on July 13, 1881, the son of Dr. Eugene A. Chapman and Agnes McClure Chapman. He was graduated from the Union Academy in Belleville in 1898 and attended Syracuse University from 1898 to 1901. He received his degree of Doctor of Medicine from the University of Michigan in 1905. On Dec. 29, 1908 he married Miss Marion E. Clapp, of Ithaca, N. Y.

Dr. Chapman began practice at Watertown, N. Y., in 1905. He passed an examination for, and was appointed to, the position of medical intern at the Utica State Hospital in 1906, where he served until his transfer to the Binghamton State Hospital in 1908, after passing a promotion examination for the grade of junior assistant physician. At Binghamton he served under Dr. Charles G. Wagner, one of the most progressive state hospital superintendents of his time, and was promoted to assistant physician and then to senior assistant physician. In 1911 he took a postgraduate course at the New York Psychiatric Institute, under the teaching of Dr. August Hoch. Most of his experience in Binghamton was in the reception service, where his interests rapidly widened to include both the organic and the psychologic aspects of mental diseases. He was not satisfied with the formal psychiatry of that period but sought more dynamic concepts. He was among the first of American psychiatrists to recognize the value to psychiatry of Sigmund Freud's contributions. The excellence of his clinical work and his administrative ability attracted the attention of Dr. William A. White, who, in August 1916, appointed him to the position of first assistant physician to St. Elizabeths Hospital, Washington, D. C.

At St. Elizabeths he came into an environment ideally suited to his inclinations and enthusiasms. He took over a large part of the administration of the hospital, thus affording Dr. White a better opportunity to continue the research and literary work which contributed so greatly to the advance of psychiatry in America. The experience thus gained by him, together with his teaching, eminently qualified him for the position of superintendent of the Sheppard and Enoch Pratt

Hospital, Towson, Md., to which he was appointed in 1920 to succeed Dr. Edward N. Brush, a former president of the American Psychiatric Association. Under Dr. Chapman's management and guidance (1920-1948), this excellent hospital has been enlarged, improved and equipped with modern facilities.

Dr. Chapman's work as a teacher of psychiatry began while he was in St. Elizabeths Hospital in 1916, when he was appointed instructor in psychiatry in George Washington University, serving in that position until 1920. Soon after assuming the superintendency of the Sheppard and Enoch Pratt Hospital, he was appointed associate professor of psychiatry in the University of Maryland School of Medicine and in 1923 was made professor of psychiatry there, continuing to serve in that capacity until his death.

In 1918 Dr. Chapman was commissioned a Major in the Medical Corps, United States Army, Division Psychiatrist for the Sixth Division, and was on occupation duty in Germany as assistant consulting neuropsychiatrist. During World War II he served as a consultant in psychiatry, Medical Advisory Board, United States Public Health Service in Washington, D. C., in 1940; served on a special committee at Selective Service Headquarters in Washington, D. C., and did induction work from 1940 to 1945, for which he was decorated and awarded the Selective Service Medal. He was certified in psychiatry by the American Board of Psychiatry and Neurology in 1937.

He was a member of the American Medical Association, the Maryland Medical Association, the Baltimore County Medical Association (president in 1945) and the Southern Medical Association; a fellow of the American Psychiatric Association (president, 1937-1938); a member of the American Psychopathological Association (president, 1928); a member of the American Psychoanalytic Association; a member of the board of directors of the Mental Hygiene Society of Maryland, and a member of the board of trustees of the Severn School, Severance Park, Md.

He was a Republican, a Presbyterian, a Mason and a member of the Maryland Club (Baltimore) and of the Army and Navy Club (Washington, D. C.).

What a record he made! For over forty-two years he devoted all of his professional interests to psychiatry. His contributions to psychiatry are well known. As an educator, a clinician and an administrator his influence on psychiatric progress has been impressive. His presidential address to the American Psychiatric Association in June 1938 well expressed his insight into the problems confronting psychiatric practice; he said: "There rests upon us the heavy responsibility for a broad, genuine (no longer haphazard) educational program. Medical leadership must be furnished, trained personnel must be produced."

He practiced what he preached by teaching psychiatry to medical students and by exerting a still greater influence on the young men whom he gathered about him to constitute his medical staff. Many of these physicians have won distinction in the psychiatric field.

It is difficult to summarize Ross Chapman's jovial personality in words. He had a multitude of friends; he was a boon companion socially or on a vacation outing; he loved his fellow men and was generous to a fault, always with helpfulness, understanding and sympathy when help was needed. His wise councils and his stimulating influence will be sadly missed in the psychiatric field.

WILLIAM J. TIFFANY, M. D.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

NERVOUS SYSTEM AND REGENERATION OF THE FORELIMB OF ADULT TRITURUS: V. INFLUENCE OF NUMBER OF NERVE FIBERS, INCLUDING A QUANTITATIVE STUDY OF LIMB INNERVATION. MARCUS SINGER, J. Exper. Zool. **101**:299 (April) 1946.

As a basis for the further analysis of the importance of quantity of innervation for forelimb regeneration in Triturus viridescens, experiments were devised to enable a determination of the fiber value (total count; sensory fiber number) of each brachial spinal nerve and the nerve component at the selected amputation level. Using the results of these anatomic studies, the author performed specific operations on the brachial nerves in order to obtain different fiber number values. Twenty-three series were elaborated, ranging from a high to a very low fiber number value.

The results show that the threshold above which regeneration of the forelimb is always obtained is about one half of the fiber content of the amputation surface, while the lower limit (below which regeneration is absent) has a value of approximately one third. Regeneration does not occur in all instances within this threshold range.

Although each of the three brachial spinal nerves is active in the regeneration process, the effectiveness of each individual nerve is directly related to its quantity of nerve fibers.

The sensory supply is the only component whose fiber quantity meets the threshold requirements. When the sensory fiber value is reduced, there are not enough remaining sensory fibers to supply the neural stimulus needed for regeneration. The motor quantity of the normal limb is too low to provide information on motor activity in these experiments, but there is support for the view previously reached by the author that motor fibers also possess the neural quality essential for limb regeneration. The small sympathetic nerve supply was retained as a constant throughout these experiments.

That all nerve fibers, irrespective of their origin, may possess the neural quality necessary for the regeneration of the extremity is discussed. The role of the individual nerve fiber in the quantitative expression is also discussed.

REID, New Brunswick, N. J.

ROLE OF NUCLEUS AND CYTOPLASM IN DEVELOPMENT OF PIGMENT PATTERN IN TRITURUS. HOWARD C. DALTON, J. Exper. Zool. **103**:169 (Oct.) 1946.

Enucleation of the fertilized egg with a micropipet resulted in homospermic merogones of Triturus torosus, Triturus granulosus and Triturus rivularis. The merogones of T. torosus, which were the only ones to develop beyond the tail bud stage, produced larvae with the normal pigment pattern for this species. Although merogones of the three species were produced in all hybrid combinations, the success varied with the combination of nucleus and cytoplasm employed, and none developed to the point of pigment production.

Haploid torosus neural crest transplanted homotopically to diploid torosus hosts produced normal torosus pigment patterns in the graft region. Haploid melanophores can thus produce normal pigment patterns when transplanted homoplastically.

That haploid melanophores can develop the donor type of pigment pattern when transplanted heteroplastically was shown by the experiments with haploid rivularis neural crest transplanted to diploid torosus hosts. Normal rivularis pigment pattern occurred in the graft region.

Haploid hybrid neural crest (cells containing torosus nucleus and rivularis cytoplasm) transplanted homotopically to diploid torosus hosts produced a pigment pattern like that of the nucleus-donor species, T. torosus. However, the number of melanophores appearing on the flank and their degree of dispersion showed a tendency toward the pattern type of the cytoplasm-donor species, T. rivularis. Hence the cytoplasmic properties determined very early in development may later become critical factors in the differentiation of a specific genetic characteristic.

REID, New Brunswick, N. J.

RESTITUTION OF THE BRACHIAL REGION OF THE CORD FOLLOWING EXCISION IN THE EMBRYO. S. R. DETWILER, J. Exper. Zool. **104**:53 (Feb.) 1947.

The data show that excision of the right half of the presumptive brachial region of the spinal cord from Amblystoma embryos in stage 21 ± (closed neural folds) may be followed by complete restitution. Excessive cellular proliferation and migration of cells from the intact contralateral half is the means by which the gap is filled in the early stages. After the establishment of a definite tube, the process is augmented by proliferation of ependymal cells on the side of operation. There is no valid evidence that cellular proliferation from the cephalic and caudal stumps of the same side contributes to the restitution.

This mode of regeneration of the brachial region of the cord follows a pattern like that observed in regeneration of the medulla and the mesencephalon after unilateral excision. Hence, in all three regions of the central nervous system, one half is totipotent for the whole in embryos with just closed neural folds.

REID, New Brunswick, N. J.

REGRESSION AND SHORTENING OF THE PRIMITIVE STREAK IN THE EXPLANTED CHICK BLASTODERM. NELSON T. SPRATT JR., J. Exper. Zool. **104**:69 (Feb.) 1947.

Extensive studies and measurements of over 800 living chick blastoderms were made to determine the processes of regression and shortening of the primitive streak. Several methods were employed: marking with powdered carbon on the epiblast cells of the explanted blastoderm; marking with carbon powder in ovo; marking with vital dyes in ovo and in vitro, and the study of normal living and normal fixed and stained blastoderms. All the methods used gave the same type of result, with but small differences attributable to the methods.

The primitive streak of the chick blastoderm is "pushed" from the scene of action by the embryo growing in front of it. The speed of this regression parallels the rate of growth in length of the embryo. As the streak moves backward, it is progressively shortened by a transformation of its posterior end into embryonic and extraembryonic ectoderm and mesoderm as the more anterior levels of the streak are moved back into the future tail region of the embryo. The node and possibly a small portion of the streak behind it become the end bud, through the activity of which the remainder of the embryo behind the twenty-seventh somite level is formed. Although the general relation of the developing embryo to the streak is now clear, a more precise analysis of this relation is necessary and will be presented by the author in another report.

REID, New Brunswick, N. J.

Physiology and Biochemistry

THE EFFECTS OF HYPOPHYSECTOMY ON GASTRIC ACIDITY OF ADULT FEMALE RATS. R. C. CRAFTS and B. S. WALKER, Endocrinology **40**:395 (June) 1947.

Crafts and Walker found that adult female rats have a spontaneous secretion of gastric juice which frequently contains free hydrochloric acid. Hypophysectomy induces a decrease in the volume of gastric secretion and an increase in the values for p_H. Rats made anemic by bleeding from the heart produced gastric juice which was of higher titratable acidity and lower p_H than that produced by hypophysectomized rats. The authors conclude that hypophysectomy induced a decrease in volume of gastric secretion which was not due to the anemia which followed hypophysectomy in the adult female rat.

FRANKEL, Philadelphia.

DISTRIBUTION OF INTRAVENOUSLY INJECTED GLUTAMATE, LACTATE, PYRUVATE AND SUCCINATE BETWEEN BLOOD AND BRAIN. J. R. KLEIN and N. S. OLSEN, J. Biol. Chem. **167**:1, 1947.

Intravenous injection of a number of substances, known to be oxidized by brain in vitro, does not maintain the electrical activity of brain or relieve symptoms of hypoglycemia in eviscerated animals. Of these substances, fructose, whose oxidation by brain in vitro follows the same pattern as that for glucose, when injected intravenously does not attain a concentration in brain that might be expected to relieve symptoms of hypoglycemia. The concentrations of lactate in brain and blood vary independently in such fashion that interchange of lactate between these tissues must be slow; consequently, intravenous injection of lactate would not be expected to provide brain with a concentration that would meet its metabolic requirements. A hypothesis that would explain the failure of intravenous injection of any substance to affect brain, although the substance may have a considerable effect in vitro, is that its rate of transfer from blood to brain is not sufficient to provide an effective concentration in brain. The concentrations of 1(+) glutamate, 1(+) lactate and succinate determined in blood plasma and brain at intervals after intravenous injection of these substances were such as to indicate that their rates of transfer from blood to brain are much less than the rate for glucose. The concentrations of these substances would not be expected to serve as a substitute for glucose in relief of hypoglycemic symptoms. After injections of pyruvate, the concentration of brain lactate increased to an extent indicating a considerable rate of transfer of pyruvate from blood to brain. Therefore, the failure of pyruvate to relieve symptoms of hypoglycemia may be due to inability of lactate oxidation to support central nervous function.

PAGE, Cleveland.

BINOCULAR SUMMATION WITHIN THE NERVOUS PATHWAYS OF THE PUPILLARY LIGHT REFLEX. L. C. THOMSON, J. Physiol. **106**:59, 1947.

It was shown that the degree of constriction of the pupil which results from the stimulation by light of the retina of a single eye was significantly less than that obtained when both eyes were stimulated. This binocular summation was equivalent to that obtained by increasing the area of the stimulating flash between two and four times and observing with a single eye throughout. This binocular summation does not appear to be influenced by activity of the cerebral cortex. The position of the summation within the neural pathways is discussed.

THOMAS, Philadelphia.

SUBTHRESHOLD POTENTIALS IN MEDULLATED NERVE. BERNHARD KATZ, J. Physiol. **106**:66, 1947.

Blair (1938) and Tasaki (1940) insisted that the nerve impulse in normal medullated axons is generated in an all or none fashion, that the effects of subliminal shocks are strictly proportional to their intensity and that a local response to a subthreshold stimulus does not exist.

The matter was reexamined by recording the subthreshold changes in potential in the frog's sciatic nerve resulting from brief single shocks. Using a small distance between the stimulating electrodes and a bridgelike arrangement of the recording leads, it is possible to reduce shock artefacts and electrotonic potentials sufficiently to permit search for a nonconducted response.

With weak shocks, up to about one-third threshold value, the local change in potential (i. e., unbalanced remainder of shock and polarization potential) increases linearly with shock intensity. Above that strength, a small local depolarization is observed, which increases more than linearly as the intensity of stimulus is raised. At threshold, the amplitude of this local negative potential is about 0.35 microvolt (mean of seventeen experiments) in the sciatic nerve. This potential is abolished by killing or deeply narcotizing the nerve.

THOMAS, Philadelphia.

ACTION OF INTRATHECALLY INJECTED ESERINE [PHYSOSTIGMINE] ON THE SPINAL CORD OF THE CAT. I. CALMA and SAMSON WRIGHT, J. Physiol. **106**:80, 1947.

The action of intrathecally injected physostigmine on the knee jerk, flexor reflex, crossed extensor reflex, "jar reflex" * and muscular tone was studied in the cat under anesthesia induced with chloralose and dextrose and in the decerebrate cat. Physostigmine increases the knee jerk, the crossed extensor reflex and the jar reflex. It increases and prolongs the after-discharges of all these reflexes. Radiation, facilitation and occlusion phenomena occur during the action of physostigmine. The drug has a variable effect on the flexor reflex, potentiating it, inhibiting it or not modifying it at all. Evidence is presented of inhibitory central effects produced or intensified by physostigmine, superimposed on and modifying the predominantly potentiating action of the drug.

THOMAS, Philadelphia.

THE NERVOUS PATHWAYS OF INTESTINAL REFLEXES ASSOCIATED WITH NAUSEA AND VOMITING. R. A. GREGORY, J. Physiol. **106**:95, 1947.

The production of nausea and vomiting in dogs provided with Thiry or Thiry-Vella loops of jejunum causes an increase in the secretion of intestinal juice. This secretory response, and the changes in intestinal motility described in a previous paper, are unaltered by bilateral splanchnicotomy. Both intestinal responses are abolished by thoracic vagotomy.

THOMAS, Philadelphia.

ACTION OF ACETYLCHOLINE IN THE SUPRAOPTIC NUCLEUS OF THE CHLORALOSED DOG. MARY PICKFORD, J. Physiol. **106**:264, 1947.

Pickford describes experiments which show that acetylcholine injected into the supraoptic nucleus of the dog treated with chloralose (a compound of chloral hydrate and dextrose) results in inhibition of the rate of flow of urine during water diuresis. This inhibition is prolonged by the addition of physostigmine salicylate to the solution injected, and no systemic changes in blood pressure can be associated with it. Physostigmine salicylate injected alone produces a similar inhibition of

* A contraction of the contralateral tibialis anticus associated with the knee jerk in some spinal preparations.

the rate of flow of urine. The injection of 0.9 per cent sodium chloride solution into the same area has, at best, a fleeting effect. Further, physostigmine and acetylcholine, injected together into one of the mamillary bodies or into the lateral portion of the hypothalamus, are without effect on the rate of flow of urine. No inhibition of the rate of flow was seen on injection of acetylcholine after the removal of the pituitary gland. All these observations were made on dogs whose kidneys had been denervated.

The results are consistent with the hypothesis that acetylcholine stimulates the cells of the supraoptic nucleus, thereby inducing the release of the antidiuretic hormone from the posterior lobe of the pituitary gland. They also show that the lateral portion of the hypothalamus and the mamillary bodies do not release an antidiuretic hormone, and that acetylcholine applied in this way does not release the hormone.

THOMAS, Philadelphia.

MEMBRANE RESISTANCE OF THE NON-MEDULLATED NERVE FIBRE. A. L. HODGKIN, J. Physiol. **106**:305, 1947.

The electrical constants of isolated axons from Carcinus maenas were measured with pulses of direct current and longitudinal electrodes. The electrical resistance of the nerve membrane varied between 2,000 and 16,000 ohms per square centimeter in excitable axons and had an average value of about 8,000 ohms per square centimeter. The specific resistance of the axoplasm was found to be about 90 ohms per square centimeter (four times sea water). The ratio of internal to external resistance per unit length was approximately 1.6. The nerve membrane was found to obey Ohm's law over a wide range of anodal currents, but showed notable deviations with relatively weak cathodal currents.

THOMAS, Philadelphia.

VAGAL NERVE FIBRE ACTIVITY FOLLOWING MULTIPLE PULMONARY EMBOLISM. E. G. WALSH, J. Physiol. **106**:466, 1946.

Walsh investigated the behavior of single vagal afferent fibers in cats and rabbits, in an attempt to discover the group responsible for the rapid breathing that follows potato starch embolism of pulmonary capillaries. It was shown that after embolism the peak frequencies of discharge of single stretch endings in artificially ventilated animals showed no significant change. Sensitivity of stretch endings in spontaneously breathing animals was unchanged. The discharge of some endings, apparently situated on the walls of blood vessels, was increased.

The author concludes that the accelerated breathing following pulmonary embolism is probably not due to increased frequency of discharge of stretch receptors.

THOMAS, Philadelphia.

SYNTHESIS AND ACCUMULATION OF ACETYLCHOLINE AT MOTOR END PLATES. R. J. S. MCDOWALL and A. Z. SHAFEI, J. Physiol. **106**:2P, 1947.

The liberation of acetylcholine at motor nerve endings is now well recognized. The authors have demonstrated that conditions which reduce or increase the synthesis of acetylcholine in brain tissue and brain extracts affect in a similar way the responses to nerve stimulation of the phrenic nerve–diaphragm preparation of Bülbring (1946) suspended in various modifications of Tyrode's solution. Thus, they are decreased by calcium and dextrose and are increased when calcium and dextrose are reduced. The response to direct muscular stimulation is not so much affected and is not always parallel. It is, however, present after curare.

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An accumulation of acetylcholine at resting nerve endings is suggested by the occurrence, after a period of rest, of a few supernormal contractions with delayed relaxation at the beginning of a series of nerve stimulations, but this is less evident when the muscle is stimulated directly after a similar rest. These results are made still more evident by physostigmine, which prevents the destruction of acetylcholine, especially when dextrose is absent and calcium is deficient.

THOMAS, Philadelphia.

Neuropathology

ETIOLOGY AND PATHOGENESIS OF ACUTE SPORADIC DISSEMINATED ENCEPHALOMYELITIS AND MULTIPLE SCLEROSIS. M. S. MARGULIS, V. D. SOLOVIEV and A. K. SHUBLADZE, J. Neurol., Neurosurg. & Psychiat. **9**:63 (April) 1946.

Margulis and others report 2 cases of acute disseminated encephalomyelitis in which two strains of filtrable viruses were isolated. In the first case, the clinical course was one of acute onset with remissions and exacerbations and eventual recovery. After inoculation with the patient's blood and spinal fluid, a virus was isolated from the blood of albino mice. In the second case, the illness ended fatally and autopsy disclosed changes in the brain compatible with the diagnosis of acute disseminated encephalomyelitis. The lesions were miliary necrotic and demyelinating foci, showing an inflammatory vascular reaction and proliferation of microglia and of astrocytes throughout the white substance of the cerebral hemispheres, brain stem and medulla oblongata. After inoculation of albino mice with the cerebral substance of this patient, a virus was isolated.

Albino mice, puppies, rats, guinea pigs and rabbits were then inoculated with both strains of virus. The changes produced in these animals closely resembled, both clinically and pathologically, those of acute disseminated encephalomyelitis and of multiple sclerosis. The virus strains showed distinct differences from those of herpes encephalitis and spring-summer encephalitis of Far East Siberia, as well as various spontaneous neuroinfectious diseases of mice. The method of spread of the virus was observed experimentally to follow two patterns, namely, hematogenous and neural. The former was considered to be the chief mode of spread, whereas spread by the latter route occurred later and progressed at a lower rate.

The virus strains were then mixed with the serum obtained from patients with acute disseminated encephalomyelitis and with multiple sclerosis. In 70 per cent of the former and in 50 per cent of the latter the results of the neutralization tests were positive. On the basis of these findings, the authors conclude that acute disseminated encephalomyelitis and acute multiple sclerosis are identical disorders. The differences in the clinical and pathologic features of acute disseminated encephalomyelitis and of chronic multiple sclerosis depend only on the acuteness and chronicity of the evolution of the changes. The similarity in the serologic data suggests that acute disseminated encephalomyelitis is the acute form of chronic multiple sclerosis, at least in cases in which the neutralization test has proved positive. In those cases in which the serologic reactions were negative, either another agent or a difference in the antigenic structure of the same agent may be assumed.

Four patients with acute disseminated encephalomyelitis and 19 patients with multiple sclerosis were then subjected to specific vaccine therapy. The results showed clinical improvement with increase in antibodies in the blood in all the patients with acute disseminated encephalomyelitis and in 11 of the patients with multiple sclerosis.

N. MALAMUD, Los Angeles.

A Cortical Anomaly with Some Porencephalic Features. Charles Davison and Arnold P. Friedman, J. Neuropath. & Exper. Neurol. **5**:225 (July) 1946.

Davison and Friedman report in detail the history and necropsy observations in the case of a man aged 74 who died as the result of adenocarcinoma of the rectosigmoid region. Examination of the brain revealed the presence of a cavity which extended from the middle half of the right temporal convolutions to the orbital convolutions, exposing the island of Reil. There were no areas of softening or destruction of the gray or the white matter. The cavity communicated only with the subarachnoid space, and not with the ventricular system. The patient had led an active life, and there were no abnormal neurologic signs.

There was evidence of arteriosclerosis. For six months prior to his death, the patient experienced bouts of syncope, giddiness, lapses of memory and confusion. At necropsy, although the vessels in the insula showed definite atherosclerotic changes, areas of softening in these convolutions were not encountered. It is doubtful whether the few calcified vessels observed in the meninges were responsible for this porencephalic anomaly. The small area of demyelination in the right optic radiations and cerebellum had no bearing on the pseudoporencephaly. This case, unusual in nature, must be considered as a malformation.

Guttman, Wilkes-Barre, Pa.

Concerning Gangliogliomas of the Brain. Percival Bailey and Helen Beiser, J. Neuropath. & Exper. Neurol. **6**:24 (Jan.) 1947.

Bailey and Beiser attempted to determine the incidence of brain tumors in which neurons form an integral part of the neoplastic tissue. Globus has reported that they are relatively frequent. Bailey and Beiser studied 162 consecutive cases of glioma of the brain and observed 2 cases in which neurons seemed to form an integral part of the neoplasm. One case was that of a man aged 51 with a glioma involving the left temporal lobe. The other was that of a man aged 61 with a glioma which lay in the left hemisphere at the level of the pineal body, just lateral to the lateral ventricle, and extended deep into the occipital lobe and forward irregularly to the level of the optic chiasm. The neoplasms measured 6.5 and 6 cm., respectively.

The authors, in commenting on the first case, state that the neurons in the tumor seemed to be an essential constituent of its structure. They were evenly distributed throughout, with healthy nuclei, and no evidence was found of inclusion of normal cerebral tissue in the neoplasm, which seemed to have grown by expansion. No fully developed astrocytes or myelin sheaths were observed in the growth. The neurons were in all stages of development and formed only unmyelinated processes; rarely were more than small, scattered tigroid masses seen, and the vast majority of the neoplastic cells were bipolar spongioblasts.

The neurons in the second case were regarded as inclusions. This tumor, unlike the first, had no sharp margin but shaded off into the surrounding tissue, so that it was often impossible to determine where the neoplastic tissue terminated. There was a broad zone of gliosis, with swollen cytoplasmic astrocytes. One feature was interesting: Even at some distance from the apparent margin one could find cuffs of astroblasts around blood vessels. The authors are unable to reach a conclusion concerning the origin of these cuffs of cells, but are inclined to believe that they did not reach their peripheral position by spread along the vessel walls but, rather, that they represent a malformation, on the basis of which the neoplasm developed.

It is the conviction of Bailey and Beiser that neuroepithelial tumors of the brain in which neuroblasts develop as an integral part of the neoplasm are rare.

Guttman, Wilkes-Barre, Pa.

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Diseases of the Spinal Cord

PARAPLEGIA FOLLOWING WAR. E. H. BOTTERELL, A. T. JOUSSE, C. ABERHART and J. W. CLUFF, Canad. M. A. J. **55**:249 (Sept.) 1946.

During the period of February 1945 to June 1946, Botterell and his associates observed 103 patients with post-traumatic paraplegia with stable spinal cord who were returned from overseas and were treated in Toronto at a center fully equipped and specially staffed to deal with all aspects of treatment and retraining. Forty-nine patients presented complete injuries of the spinal cord, while 54 had incomplete injuries, particularly in the lumbar and sacral regions. Death occurred in 7 instances and was considered to be due primarily to disturbances of nutrition, with genitourinary sepsis as a contributory factor. Treatment of the paralyzed bladder in these 103 patients, while overseas, consisted of suprapubic cystotomy in 77 and urethral drainage in 17; 9 had but transient retention, requiring catheterization on a few occasions. At the center in Canada, tidal drainage remains the treatment of choice. Of the 77 cystotomies, 61 have been closed, 24 by operation and 37 by healing following institution of urethral drainage by a retention urethral catheter. In patients in whom infection with gram-negative, urea-splitting organisms was rife, administration of streptomycin was of substantial value and was continued until the suprapubic wound was healed and the urethral catheter removed. Anterior rhizotomy was performed on 5 patients in whom the mass flexion reflex was disabling, and all improved substantially. In 16 of 20 patients, sacral, trochanteric and ischial pressure sores were successfully closed with full thickness skin grafts. Bilateral section of the tract mediating pain proved of great value in the treatment of 4 patients with disabling pain who had lesions involving the cauda equina. Retraining commences while the patient is still in bed and gradually progresses. By grasping a bed frame exerciser, the patient may be enabled to turn himself independently at two hour intervals by day and by night. Long leg braces of chrome molybdenum have been evolved and are put forward as being particularly suitable for paraplegic patients. Custom-made boots of modified hockey cut type, light in weight and particularly flexible, are recommended as a means of preventing pressure sores of the feet.

J. A. M. A.

EXTRASPINAL LUMBAR MENINGOCELE. ROBERT C. PENDERGRASS, A. EARL WALKER and JOHN P. BOND, J. Neurosurg. **4**:80 (Jan.) 1947.

Pendergrass, Walker and Bond report a case of a paraspinal meningocele in the lumbar region with a visible, palpable mass in the loin. A 32 year old soldier was admitted to the hospital complaining of pain in the lower portion of the back, headache when bending over and suddenly raising up and a tender mass in the left loin. He had been well until one year before examination, when he had been crushed between a tractor and a truck. Two months previous to his present admission a retrograde pyelogram was made, which revealed a displaced left kidney and ureter. Aspiration of the mass in his loin at this time revealed a clear, colorless fluid, and air subsequently injected into the sac was seen in the cranial cavity in the roentgenogram. Examination of the patient showed a large, fluctuant mass in the left lumbar region, extending from the twelfth dorsal to the fourth lumbar vertebra. Neurologic examination gave essentially negative results. Roentgenograms of the spine showed absence of the spinous processes of the eleventh and twelfth thoracic vertebrae and of the transverse processes of the first, second, third and fourth lumbar vertebrae on the left side. These transverse processes were found in the flank at the outer aspect of the mass. At the time of the first operation an attempt was made to close the opening with sutures and patch it with flaps

from the wall of the sac. This was unsuccessful, and two months later the second operation was performed. Through a hemilaminectomy incision, the neck of the meningocele was isolated at the twelfth thoracic vertebra, and the dural sleeve was then resected and closed as it passed through the intervertebral foramens. Three months following an uneventful convalescence, the mass in the flank had disappeared, there was no impulse on coughing and the patient no longer complained of headache due to sudden change in position.

TOZER, Philadelphia.

EPENDYMOMA OF THE CAUDA EQUINA. R. CARRILLO, Arch. de neurocir. **1**:241 (April-June) 1944.

Carrillo reports the case of a man aged 35 who had been ill for five years. For two years he had lumbar and sciatic pain, which did not respond to treatment. During the next two years he had paresthesias in the lower limbs, with weakness and intensification of pain. For a year before his admission he had sphincteric disturbances. Examination disclosed flaccid paralysis in the lower limbs with areflexia and saddle and radicular sensory changes. There was also evidence of involvement of the conus. Operation showed a tumor involving the cauda equina. Histologic study of the tumor revealed an ependymoblastoma mucosa.

N. SAVITSKY, New York.

EYE SYMPTOMS IN POLIOMYELITIS ANTERIOR ACUTA. P. KINDT and K. KNUDTZON, Acta ophth. **24**:295, 1946.

Kindt and Knudtzon found that during the extensive epidemic of poliomyelitis in 1944, when 279 patients with this disease were admitted to the Frederiksberg Hospital, a rather large number had ocular symptoms. Of the 37 patients presenting symptoms referable to the brain stem, 23 had ocular symptoms. In 20 of the 23 patients the symptom which occasioned the summoning of the eye specialist was diplopia or, in a few cases, dimmed vision or flickering before the eyes. Double vision was constant or periodic in most cases. Paresis of the extraocular muscles was found in only 10 of the 20 patients who complained of double vision or dimmed vision. In 3 patients diplopia was one of the primary symptoms; in most of the others the ocular symptoms appeared between the fourth and the eleventh day. All the ocular symptoms disappear completely, or almost completely, without special treatment in patients who survive the disease.

J. A. M. A.

ACUTE ANTERIOR POLIOMYELITIS IN PREGNANCY. P. HORSTMANN, J. IPSEN and H. C. A. LASSEN, Nord. med. (Hospitalstid.) **30**:807 (April 12) 1946.

Horstmann and his associates state that of the 62 women, aged from 20 to 34, with poliomyelitis treated in Blegdam Hospital during the 1944 poliomyelitis epidemic in Copenhagen, 20 were pregnant; 15 were in the first half of the pregnancy. Three of these patients died in the acute stage of the disease; abortion occurred in 4, and the infant died shortly before or after delivery in 2 instances, while 11 children were born, all of whom developed normally after birth. Since the frequency of pregnancy in poliomyelitis here is about three times as high as might be expected from the birth rate of the population at the time, mere coincidence is unlikely. No corresponding accumulation of cases of pregnancy in poliomyelitis has previously been observed at the hospital. No satisfactory explanation of the phenomenon was found. The increased incidence of poliomyelitis in adult age in recent years probably explains the susceptibility to poliomyelitis in pregnancy. In the 1943 poliomyelitis epidemic in Bleking, 21 of the 53 women between the ages of 19 and 47 who had the disease were pregnant (Dhunér: *Nord. med.* **24**:2187, 1944).

J. A. M. A.

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Vegetative and Endocrine Systems

ACTIVATION OF THE ANTERIOR HYPOPHYSIS BY ELECTRICAL STIMULATION IN THE RABBIT. J. E. MARKEE, CHARLES H. SAWYER and W. HENRY HOLLINSHEAD, Endocrinology **38**:345 (June) 1946.

By means of electrical stimulation of the cervical portion of the sympathetic chain, vagus nerves, hypothalamus and anterior lobe of the pituitary gland of rabbits, further information on the relation of the nervous system to the anterior lobe of the hypophysis was sought. The criterion used for successful activation of the anterior lobe of the pituitary gland was the production of ovulation, indicating the release of luteinizing gonadotropic hormone, such as normally occurs in the rabbit after coitus. Negative results were obtained after stimulation of the cervical portion of the sympathetic trunk in 27 unanesthetized mature female rabbits and after cervical stimulation of the vagus nerve in 22 animals. Direct unipolar stimulation of the anterior lobe of the pituitary gland in 19 animals induced ovulation only when stimulation was sufficiently intense to produce evidence of considerable spread to the central nervous system. Bipolar stimulation of the pituitary gland failed to effect ovulation in 7 rabbits and was not accompanied with evidences of spread to the central nervous system,. Bipolar stimulation of the hypothalamus, however, under the identical conditions found ineffective on the hypophysis, induced ovulation in 3 of 4 animals.

The authors conclude that their experiments confirm the observations of other workers that the hypothalamus plays a major role in the release of luteinizing hormone from the anterior lobe of the hypophysis. However, they interpret the difference in the electrical excitability of the hypophysis and of the hypothalamus as indicating that the latter does not exert a direct neural control over the anterior lobe of the hypophysis and suggest that a humoral factor is responsible.

A. E. RAKOFF, Philadelphia.

ESTROGEN IN LATE PREGNANCY MARE SERUM AND OVARIAN INHIBITION. H. H. COLE, Endocrinology **39**:177 (Sept.) 1946.

Cole attempts to determine the cause of ovarian inhibition produced by late pregnancy mare serum. To accomplish this aim, he studied experimentally the antigonadotropic activity of late pregnancy mare serum and ovarian inhibition and stimulation with both alpha estradiol benzoate U. S. P. and late pregnancy serum.

Since early pregnancy mare serum has a high gonadotropic activity, the possibility of an antigonadotropin in late pregnancy mare serum which can produce an inhibitory effect was investigated by comparing the ovarian response of equine gonadotropin alone with equine gonadotropin plus late pregnancy serum. The data indicate that, although the serum has an inhibitory effect on ovarian development when given alone, it does not appreciably depress the ovarian response to injected gonadotropin.

Cole then proceeded to determine whether ovarian inhibition was produced by the small amount of estrogen in the blood. For purposes of comparison, the ovarian response to alpha estradiol benzoate was determined. This substance produced ovarian inhibition in doses just below the amount necessary to produce full estrous smears in all the experimental rats on the fourth day after initial injection. The relation between the vaginal smear picture and ovarian inhibition is comparable to that found with late pregnancy mare serum. The estrogen was then extracted from late pregnancy mare serum and injected into immature rats. Both ovarian inhibition and stimulation were obtained with the extract; the nature of the response depended on the dose, smaller doses producing inhibition.

The effect of late pregnancy mare urine, which has a higher estrogenic potency than pregnancy serum, was compared with that of the latter. The urine produced inhibition at lower dosage levels than does untreated pregnancy serum in comparable physiologic doses.

The author concludes that the inhibitory effect of late pregnancy mare serum on ovarian development depends on the estrogen present. The estrogen stimulates the ovary directly over short periods and depresses the ovary indirectly by inhibiting the secretion of gonadotropin by the pituitary.

FRANKEL, Philadelphia.

COMPARISON OF THE SPERMATOGENIC AND ANDROGENIC PROPERTIES OF TESTOSTERONE PROPIONATE WITH THOSE OF PITUITARY ICSH [INTERSTITIAL-CELL-STIMULATING HORMONE] IN HYPOPHYSECTOMIZED 40-DAY OLD MALE RATS. M. E. SIMPSON and M. E. HERBERT, Endocrinology **39**:281 (Nov.) 1946.

In a previous communication (Simpson, Li and Evans, 1944) it was reported that the interstitial-cell-stimulating hormone (ICSH) of the pituitary gland stimulated the testicular tubules of male rats hypophysectomized at 40 to 43 days of age at doses so low that the interstitial cells were not appreciably affected and the seminal tubules and prostate were not prevented from regressing in weight to the level of those of the hypophysectomized controls.

In this study, Simpson, Li and Evans compared the spermatogenic and androgenic potencies of testosterone propionate in similarly treated male rats. Graded doses of testosterone propionate, ranging from 2.5 to 0.010 mg. in 0.1 cc. of sesame oil, were injected subcutaneously into the experimental animals for fifteen days, beginning on the day of hypophysectomy. It was found that there was some stimulation of the testicular tubules with daily doses as low as 0.05 mg.; when 0.1 mg. was injected, spermatozoa were present in the tubules, as in the normal 55 day old rat. However, the male accessory organs were also stimulated in a similar degree by these doses.

The authors assume that the stimulation of spermatogenesis by anterior pituitary is mediated through the male sex hormone produced by the interstitial cells, which are stimulated by interstitial-cell-stimulating hormone. Because of the experimental evidence bearing out this view, a further assumption must be made; namely, that interstitial cells not producing morphologic evidences of stimulation produce a steroid having a different physiologic action than testosterone propionate, being more effective in stimulation of testicular tubules and less effective in stimulation of the accessory organs of the male than is testosterone propionate. The authors make a reservation in accepting interstitial-cell-stimulating hormone as the complete pituitary gonadotropic hormone in the male.

FRANKEL, Philadelphia.

MENTAL ANOREXIA AND SO-CALLED HYPOPHYSIAL CACHEXIA. J. DECOURT, Paris méd. **1**:249 (June 8) 1946.

Decourt reports 13 cases of a syndrome consisting of amenorrhea, anorexia and rapid cachexia in girls and women between the ages of 15 and 32 years. The loss of body weight varied from 11 to 33 Kg. Twelve of the patients recovered as a result of psychic therapy, and particularly of the resulting resumption of absorption of food in the absence of any opotherapy. The incidence of Simmonds disease, conceived as a purely organic disorder due to primary atrophy of the anterior lobe of the pituitary, is low. A large number of cases which were reported as instances of Simmonds disease should be reconsidered

on the concept of mental anorexia. The latter condition results primarily from a psychic disorder, although a disorder of the diencephalohypophysial function may play a part in the physiopathology of mental anorexia and may explain the inaugural character of the amenorrhea. In considering mental anorexia as a psychoendocrine disorder, its origin, as well as its therapy, remains psychic. Complete recovery occurs as a result of mental reeducation associated with isolation, rest in bed and resumption of food absorption, provided this treatment is not instituted too late. The return of menstruation within three to five weeks in some of the author's cases may have been the result of psychotherapy, rather than of rebuilding by the nutritive substances. Irreparable damage may have occurred prior to late treatment in cases in which amenorrhea persisted in spite of the restoration of the nutritional balance. Atrophy of the anterior lobe of the pituitary may be not only the cause, but the sequel, of denutrition.

J. A. M. A.

Treatment, Neurosurgery

ALEXANDER'S RABBIT SERUM IN TREATMENT OF INFLUENZAL MENINGITIS: EVALUATION OF ITS USE IN CONJUNCTION WITH SULFONAMIDE COMPOUNDS. K. H. BECK and F. R. JANNEY, Am. J. Dis. Child. **73**:317 (March) 1947.

Beck and Janney review observations on patients with influenzal meningitis who were admitted to the Milwaukee Children's Hospital from January 1939 to April 1946, the span of time since Alexander's serum has been available and sulfonamide compounds have been given in massive doses. Previous to this time only 3 of 66 patients with proved influenzal meningitis had survived. Of 45 patients treated during the period when Alexander's serum was available, 24 died and 21 recovered, but 9 of 24 fatalities occurred within the first twenty-seven hours after hospitalization and thus cannot be considered in judging the efficacy of immune rabbit serum in combination with sulfonamide drugs. Of 22 patients who were treated adequately according to Alexander's standards, 19 recovered and 3 died. Of 9 patients treated with sulfonamide drugs and without serum therapy, 2 lived and 7 died. The diagnosis of influenzal meningitis must be made early in order to combat it effectively with rabbit serum and sulfonamide drugs. The sulfonamide drugs must be given in high concentrations and by the intravenous or subcutaneous route. Serum should be preceded by intravenous administration of fluids, so that the free-floating, type-specific carbohydrate of the organism is eliminated from the blood stream and the dehydration alleviated. Alexander's anti-influenza rabbit serum (administered according to her recommendations) combined with sulfonamide drugs is 85 per cent efficient in cases in which therapy is instituted before the patient is moribund. To date, it is the only efficient method for treating meningitis due to Hemophilus influenzae type B.

J. A. M. A.

TREATMENT OF H. INFLUENZAE MENINGITIS. H. E. ALEXANDER, J. M. Soc. Michigan **46**:193 (Feb.) 1947.

Alexander states that streptomycin is the most effective single antibacterial agent against Hemophilus influenzae. Since it is bactericidal, its action is rapid and effective against large bacterial populations, both in vivo and in vitro. Streptomycin, like all other single therapeutic agents, is limited if the infection is of sufficient severity; resistance of the organisms is the chief cause of failure. Experimental evidence and the response of 1 patient suggest that this defect may be overcome if sulfadiazine is used in conjunction with streptomycin; the two agents

have different modes of action, and therefore organisms resistant to one can be expected to be sensitive to the other. Whether in some patients specific anti-influenza serum is needed cannot be answered from the limited experience. There is suggestive evidence that the incidence of residual cerebral damage is less when all three therapeutic agents are used together initially, rather than in sequence after a trial of each separately.

J. A. M. A.

NERVE END SEPARATION FOLLOWING SUTURE: RESECTION OF THE NECK OF THE FIBULA IN SUTURE OF THE PERONEAL NERVE. K. E. LIVINGSTON, W. K. LIVINGSTON and DON ANDRUS, J. Neurosurg. **4**:16 (Jan.) 1947.

Livingston, Livingston and Andrus report over 300 cases of nerve lesions requiring surgical procedure for approximation. In 10 cases resuture was required because of separation at the suture site. In 9 of these cases the peroneal nerve was involved. The high incidence of disruption in this nerve is accounted for by a high fixation of the distal segment to the muscles and a relatively short over-all length of the nerve. The authors found that if the neck of the fibula was resected for a distance of 6 to 8 cm. the nerve ends could then be anastomosed with less tension. This was done in all 9 cases, in 3 of which the nerve was subsequently disrupted and had to be resutured. Disabilities or adverse symptoms were not noted from the loss of this segment of the fibula.

TOZER, Philadelphia.

OBSERVATIONS ON THE USE OF TANTALUM FOIL IN PERIPHERAL NERVE SURGERY. NATHAN CROSBY NORCROSS and JOHN T. BAKODY, J. Neurosurg. **4**:69 (Jan.) 1947.

Norcross and Bakody report their observations in 20 cases of peripheral nerve suture in which unannealed tantalum foil cuffs were used to surround the sutured sites. Scarring, in the form of circular, constricting adhesive bands, was constantly found at the upper and lower extremities of the cuff. In many instances the cuff was so tightly adherent to the underlying nerve that dissection of the foil from the nerve was extremely difficult. At times it was impossible, necessitating complete resection and fresh anastomosis. Fragmentation of the cuff led to an increase in extraneural scarring, a change not noted in the use of annealed foil. It is recommended that use of unannealed tantalum foil be confined to peripheral nerve anastomosis in which secondary suture is to be performed and that in these cases it should not be left in place more than six weeks.

TOZER, Philadelphia.

RESULTS OF TREATMENT OF RECURRING CONVULSIONS (EPILEPSY). HADDOW M. KEITH, Proc. Staff Meet., Mayo Clin. **22**:14 (Jan. 8) 1947.

Keith attempted to compare the results of drug therapy with those of ketogenic diet. Of 300 patients with epilepsy examined in 1940 and 1941, 149 were found to have idiopathic epilepsy, or, as the author states, "there were 149 patients who had no handicap but the convulsions and who were satisfactorily treated for four to five years." Thirty-seven of the 149 patients received ketogenic diet alone. Of these, 10 (27 per cent) remained completely well, 16 (43.2 per cent) were improved and 11 (29.7 per cent) were not helped. Of a group who received ketogenic diet plus drugs, 4 (26.7 per cent) remained well, 3 (20 per cent) were improved and 8 (53.3 per cent) were not helped.

Of 48 patients who received phenobarbital alone, 6 (12.5 per cent) were well, and 31 (64.6 per cent) improved for periods of a few months to four years.

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Of 50 patients who received "dilantin sodium" (diphenylhydantoin sodium U. S. P.) alone, 6 (12 per cent) remained well, 19 (38 per cent) were improved and 25 (50 per cent) were not helped.

A group of 26 patients received phenobarbital and "dilantin sodium." Of these, 3 (11.5 per cent) were well, 12 (46.2 per cent) were improved and 11 (42.3 per cent) received no help.

Of another group of patients given the ketogenic diet alone or with drugs, 35.2 per cent remained well for periods of four to twenty-two years, and 18.4 per cent were definitely improved.

"Thus, by means of a ketogenic diet 53 per cent of the patients treated who had so-called 'idiopathic' epilepsy were influenced favorably and 35 per cent have been well for long periods (four to twenty-two years)." ALPERS, Philadelphia.

THE SUPRASPINATUS SYNDROME. J. R. ARMSTRONG, Lancet **1**:94 (Jan. 18) 1947.

Armstrong reviews 89 cases of the supraspinatus syndrome, in 31 of which acromionectomy was performed. This syndrome is the commonest cause of pain in the shoulder and is characterized by a history of trauma, pain at an angle between 60 and 120 degrees on abduction of the humerus, splinting of the humerus and moving of the entire scapula when the painful arc is reached, and local tenderness on deep pressure over the supraspinatus tendon.

The pain occurs in the middle range of abduction of the humerus because that is the position at which the supraspinatus tendon and its bursa are pressed against the acromion. If there is a lesion of either tendon or bursa, this pressure causes pain and a reflex muscular spasm. There may be a persistent aching of the shoulder, which may include the whole outer side of the arm and dorsum of the forearm, or even the neck, or sharp stabbing pains, in addition to those elicited by movement of the joint. Disuse of the limb may cause periarticular adhesions and true limitation of movement.

Except when calcified deposits were present, two thirds of the patients recovered in from one to three months, irrespective of treatment. Methods of treatment included immobilization of the shoulder with splints, active exercises, local infiltration, application of heat and diathermy and manipulation of the shoulder under general anesthesia. In those cases in which there were calcified deposits in the tendon, or there was no improvement on conservative treatment in two to three months, acromionectomy was done. In this procedure the author states that it is essential to excise the acromion as far medially as, and including, the acromioclavicular articulation. In the 2 cases in which results were not satisfactory, insufficient bone was removed.

At operation 15 patients were found to have tendinitis and bursitis, 6 had calcified deposits in the supraspinatus tendon (shown by roentgen examination), 5 had tears in the tendon and 5 had primarily bursitis. The author cautions that when there is true limitation of movement, acromionectomy should not be performed before all adhesions have been broken down by exercises. He describes his operative technic and states that postoperatively the arm should be immobilized for a few days, and in about a week active exercises started. MADOW, Philadelphia.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Irving H. Pardee, M.D., President, New York Neurological Society, in the Chair
Combined Meeting, May 13, 1947

Results of Treatment with Neostigmine and Trimethadione in Fifty Cases of Spastic Neurologic Disease. Dr. Peter G. Denker and Dr. Laurence I. Kaplan (by invitation).

Fifty cases of various spastic neurologic conditions, including hemiplegias, paraplegias, miscellaneous lesions of the pyramidal tract and extrapyramidal disorders, were treated with both neostigmine and trimethadione (tridione®) to determine the therapeutic effect of these drugs on muscular spasticity. The literature on the subject was reviewed, since various favorable reports as to the beneficial effect of these drugs had been recorded. Neostigmine was administered by both the oral and the parenteral route. Trimethadione was given only orally.

No significant improvement occurred with the use of either drug. Furthermore, in 8 of 13 cases of chronic parkinsonism severe aggravation of the chief symptom, stiffness, required withdrawal of the drug. Complications were minor during treatment with each drug, and not a single case of severe leukopenia was encountered. It was concluded that neither neostigmine nor trimethadione is of any significant therapeutic value in muscle spasticity secondary to various neurologic disorders.

This article was published in full in *Bulletin of the New York Academy of Medicine* (**23**:472 [Aug.] 1947).

DISCUSSION

Dr. Benjamin Rosenbluth: For the last three or four years I have been using neostigmine, by itself or in combination with other drugs, for a variety of conditions, among which were spastic conditions, both of pyramidal and of extrapyramidal type. In cases of the extrapyramidal type, as well as in some of the pyramidal type (and the latter comprise a long series, which I have not yet tabulated), a subjective feeling of improvement at first develops. The patients report this themselves. Then the observer can see the improvement, that is, a better gait and posture and improved facility for doing things with their hands. This betterment, both subjective and objective, continues for a certain time, often for about three months, and then the condition remains in status quo and can be kept more or less at that level indefinitely with the oral administration of neostigmine. This is especially true in the cases of extrapyramidal involvement, both the encephalitic and the ordinary, or spastic, type. It has no influence on tremor, but does influence the spasticity.

Dr. Peter Denker: Dr. Harold Wolff has informed us that neostigmine has a mild analgesic action in itself; it may be that, because of this action, some patients have obtained the impression of improvement in the spastic condition with the use of this drug. Be that as it may, the results were certainly unimpressive.

The Emotional Factor in Urticaria. Dr. Foster Kennedy.

Mrs. R. F., aged 53, on March 8, 1946, while driving alone in her automobile, crossed a railroad track, the gates of which were open. However, a train struck

the rear of her car. She was flung clear of the car, which was broken up, and she was taken to a hospital by ambulance. She remembered the train's striking the rear of her car and her being flung out. However, she was physically unhurt and remained in the hospital only four hours. Since that time she has been very nervous. There are trains opposite her home, and at night the train lights come in at the window. She has slept very poorly since the accident, but she has been able to come to New York by herself and has tried to carry on the work of her small shop.

In May, for the first time in her life, she had a violent attack of urticaria, the wheals of which covered her body, necessitating hospitalization for a week. Two or three weeks later, on May 29, she was standing beside a railroad crossing when a train went by. She had a great feeling of fear, and almost immediately, i. e., within three minutes, before the closed gates had been raised, her hands and feet became immensely swollen, swollen so much that on looking at her hands she thought the skin would burst and she was unable to walk. An ambulance had to be sent for, and she was again taken to the hospital, where in a few hours giant urticaria again appeared on her body. When she is especially nervous she has "itching," but, except for the two occasions described, without the formation of hives.

Hers is a perfect case of the appearance of an allergic manifestation when the nervous system has been "triggered" by emotion.

DISCUSSION

DR. WILLIAM MAYER: Several years ago I saw in the Neurological Institute a young girl with urticarial manifestations in the palms of her hands as an equivalent of her menstrual period. In those days the girl was under emotional stress. Since then I have seen 2 similar cases. The explanation of the mechanism of the urticaria is complicated, but the surprising fact was that all 3 patients had introverted, somewhat schizoid, personalities. As a rule, such persons do not react easily with vasomotor disturbances. I have no explanation for this specific phenomenon.

DR. IRVING H. PARDEE: I observed a case similar to yours, Dr. Kennedy, that of a woman whom I knew well personally. She was in the menopausal period. For about two months she had a severe urticaria over the entire body, the eruption requiring hospitalization in an air-conditioned room and treatment by one of the best dermatologists. The periods ceased, and eventually the condition cleared up. Probably a metabolic-endocrine instability was associated with the emotional factor in this case, as well as in your case, Dr. Kennedy. Your patient had definite hyperthyroidism and was irregular in her periods throughout her life. I do not wish to belittle the element of emotion in the urticaria, but the endocrine disorder in this case only made her more susceptible to the emotional factors.

Concept of Refrigeration as a Cause of Facial Paralysis. DR. HAROLD MERWARTH.

Of 500 cases of peripheral facial paralysis, there were 351 cases of the so-called acute rheumatic, or refrigeration, type. For some time the literature has regarded chilling as a frequent cause of this idiopathic type of Bell's palsy.

This large series of cases, however, provided no such definite evidence for the direct effect of cold on the production of this paralysis. The author stated the belief that the cause of Bell's palsy is an infection, and frequency of pain and involvement of taste sense, both of which may precede actual paralysis for days, favor a continuously acting process.

DISCUSSION

DR. GEORGE H. HYSLOP: The only blood vessel supplying the facial nerve which is reasonably close to the surface is the stylomastoid artery. It supplies the peripheral, or lower, end of the facial nerve as it comes through the canal. If the commonly alleged refrigeration were to be seriously considered as even a contributing cause of Bell's palsy, one would have difficulty in accounting for the approximately 85 per cent of people with Bell's palsy who have loss or perversion of taste sense, a disorder which is due to a lesion in the geniculate ganglion. The details in Dr. Merwarth's series of cases regarding alleged exposure to cold as the reason for the development of facial palsy offer extremely unreliable evidence for this theory. No one can go through the day without being in a draft. Any local superficial vasomotor reaction would ordinarily be so slight and transient that it could have no effect on an inflammatory process originating elsewhere and involving deeper portions of the facial nerve.

Assuming that these cases which Dr. Merwarth has collected and the other series cited cover the United States area, it is apparent that climate or season is not a significant factor. A month by month analysis of his series shows that the difference in incidence for any three months is insignificant.

During the past fifteen years I have examined supposedly neurologically disabled or handicapped employees of two large railroads, and I have never seen one with facial paralysis.

DR. SAMUEL BROCK: I wish to call attention to one of the implications in Dr. Merwarth's studies, namely, that facial paralysis is a virus infection. This is a good point, because in the so-called Guillain-Barré and related syndromes, which are believed to be virus infections of the nervous system, facial paralysis is present, often bilaterally. Virus infection, therefore, is a probable cause of the "toxic" type of Bell's palsy which constitutes the greater part of his series. I should like to point out, too, that the propinquity of the facial nerve to a reservoir of infection, namely, the mouth, would make this nerve a candidate for virus infection.

DR. LEO M. DAVIDOFF: May I say just a word about an analogy in favor of a possible virus causation of Bell's palsy, and perhaps a word, too, for the preservation, in modified form, of the tradition that refrigeration has something to do with the condition? The analogy is one which every neurosurgeon has experienced; that is, after the sensory root of the trigeminal nerve has been cut, either in whole or in part, herpes simplex frequently appears; there is no reason to doubt that this infection with the virus of herpes simplex occurs in the portion of the nerve distribution which no longer has its trophic control. I wonder whether in these cases of facial palsy the virus may not affect the geniculate ganglion after cold or some other factor has predisposed the nerve to infection.

DR. BENJAMIN ROSENBLUTH: My associates and I saw 200 or 300 cases of facial palsy up to 1934, and we never noted any particular seasonal, or monthly, distribution of these cases. In some years there seemed to be a greater number of cases; in some years there would be more cases in March and in others the greater number would be in the fall; nevertheless, there was no seasonal distribution. Moreover, there seemed to be an increase in the tide of cases during epidemics of poliomyelitis. With that in mind, I asked the department of health whether they would not cooperate with us in seeing whether we could recover the virus from the cerebrospinal fluid to prove such a relation. We did cisternal punctures in about 8 cases and were unable to produce infection, and cause any symptoms of virus infection, in the monkey.

I did a bit of experimenting with refrigeration myself. Several years ago an aural surgeon advanced the theory that facial paralysis is caused by congestion of the mastoid cells and the mastoid bone. I took that suggestion seriously and in 6 or 7 cases I asked the patient to put an icebag on the mastoid bone for a few hours for two or three days. These patients had the worst cases of facial paralysis in my experience. Another case of severe facial paralysis was that of a man who applied a mustard plaster over the tip of the mastoid bone.

DR. CHARLES O. FIERTZ: The virus theory seems the most plausible, and either physical exhaustion or a chill is frequently associated with the acute infection. The combination of virus infection and refrigeration is definitely found in cases of poliomyelitis; the same association, therefore, might exist in Bell's palsy. On the other hand, I have seen a patient who had a total of seven attacks, an observation which might speak against the virus origin.

Book Reviews

Las modernas intervenciones quirúrgicas en psiquiatría. By S. Obrador Alcalde. Price, 30 pesetas. Pp. 103, with illustrations. Madrid, Spain: Paz Montalvo, 1947.

The book is a monograph on lobotomy for psychoses, a subject on which the author has been working since 1940. The book is a good review of the literature, both clinical and physiologic, which, however, adds little that is noteworthy to the account by Freeman and Watts. The most interesting part of the monograph is the description of the author's experiences with temporal leukotomy. He reports 2 cases. The first was that of a schizophrenic patient with auditory hallucinations and periods of agitation. These disturbances were not altered by removal of the lower parts of both temporal lobes. Finally a bilateral frontal leukotomy had to be performed; this largely relieved the agitation and hallucinations but produced a much more profound confusion and apathy. The results were not successful in a second similar case in which the operation was performed after partial failure of a frontal leukotomy.

Neurosurgical Pathology. By I. Mark Scheinker. Price, $8.75. Pp. 370, with 238 illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1948.

The best part of this book is the illustrations, although even some of these are dubious examples of the conditions described in the text. The author gives his concepts of swelling, injuries, tumors and abscesses of the brain and adds a chapter on hydrocephalus. None of these subjects is handled in satisfactory fashion. The attention of the reader is constantly distracted by superlatives ("tremendous, enormous, extreme") and by careless writing, such as: "The most common type of lesions is that in which the nervous parenchyma is transformed into fat granule cells." There is a silly colored drawing showing the large arteries and veins of the cerebral hemisphere coursing through the white matter to be distributed in arborizations within the cortex. In the chapter on trauma there is no mention of fat embolism, although two illustrations present the characteristic gross picture, and the case history of a crushing injury with subcutaneous emphysema should have made it obvious. Section of the brain obliquely is not helpful in photographic comparison of the two hemispheres, but there are many examples of this procedure, with correspondingly misleading descriptions. Why the author should differentiate between benign and malignant abscesses of the brain and why he should separate cerebral swelling, edema and liquefaction into three categories must remain somewhat of a mystery. The bibliography contains twenty-nine references to papers by the author.